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TREATMENT OF CARCINOMA OF THE RECTUM.¹

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THE treatment of carcinoma of the rectum does not begin and end with abdomino-perineal excision of the rectum. Both the patient and the tumour require careful study before the correct operation is decided upon, and the management after operation is as important as the actual operation itself.

A very small number of patients decline surgery or are rejected by the surgeon as unsuitable, either because the patient's condition is unsatisfactory or because the tumour is too far advanced. In a consecutive series of 186 patients with carcinoma of the rectum treated by the writer since January 1, 1957, only two refused surgery; five others were believed unsuitable for any operation except inguinal colostomy without abdominal exploration. Mostly there is little to be done for this small group of patients, but they are in need of sympathetic treatment.

LOCAL SURGERY.

A malignant polyp in the lowest third of the rectum is suitable for local removal provided the pedicle is free

of tumour. Scarborough and Klein (1948) and Helwig (1959) have described cases in which metastases have been found in regional nodes related to pedunculated adenocarcinomas, but it is a rare occurrence. Lochridge and Jackman (1958) reviewed 14 cases in which the tumour could have been treated conservatively, but in which abdomino-perineal excision was performed. One of the patients died after operation; none had involved regional nodes. In another 16 cases of similar tumours, abdomino-perineal excision was advised but rejected for various reasons. None of the 16 patients developed metastases after local treatment.

A small, low-grade, protuberant, sessile carcinoma may be also accepted for local removal if the patient is elderly or in poor health.

Surgeons with experience hold that sometimes quite large malignant tumours in the lowest third of the rectum in poor-risk elderly patients can be kept under control for long periods by diathermy to the surface of the tumour (Wittoesch and Jackman, 1958).

Local surgery is performed under general or spinal anaesthesia with the patient in either the lithotomy or jackknife position. If possible, the tumour is delivered through the anus and removed after transfixion of the pedicle, true or artificial. The patient is subsequently kept under regular observation. At each visit there is a careful digital and sigmoidoscopic examination of the site of the original tumour, with digital examination of the lymph-node area in the hollow of the sacrum.

¹A post-graduate lecture delivered in Melbourne on October 5, 1959.

In the writer's recent series of 186 patients treated since January 1, 1957, there were two instances of local excision of pedunculated adenocarcinomas. Formerly both patients would have been treated by abdomino-perineal excision. The follow-up periods in these cases are 15 months and 17 months respectively, and hence too short to allow the efficacy or otherwise of the procedure to be decided.

LAPAROTOMY.

The patient is admitted to hospital four or five days before operation. No special dietetic restrictions are imposed. No aperient is administered, but enemas are given each day. No attempt is made to sterilize the bowel with sulphonamides or antibiotics; this is unnecessary with an abdomino-perineal excision, and the resulting soft motions may be embarrassing during anastomosis in the pelvis if a restorative resection is performed. The bladder is emptied immediately prior to the operation, and in the male the catheter is left in position.

Anæsthesia is induced with thiopentone and continued with thiopentone, relaxant, and nitrous oxide and oxygen given by the endotracheal route. Spinal anæsthesia provides a more bloodless field and is preferred by some. An intravenous infusion in the right arm is continued through the operation and for two or three days afterwards.

The patient is placed in a lithotomy-Trendelenburg position by means of the St. Mark's stirrups. If there is no possibility of preserving the anal sphincter, a purse-string ligature of strong silk (16, hollow-woven) is placed around the anal orifice. If a restorative resection is contemplated, a wide self-retaining rubber catheter is inserted into the rectum. This allows the escape of mucus, faeces and flatus pushed into the rectum during dissection. The tube serves as a useful channel for irrigating the rectum with perchloride of mercury solution.

A left paramedian incision extends from just below the pubis to 2 cm. above the umbilicus. The pyramidalis muscle should be seen at the lower end, and the umbilical tendinous intersection detached from the rectus sheath.

When the abdomen is opened, the liver and upper abdominal viscera are palpated. This area is packed off and if possible not disturbed again. Moore and Sako (1959) have found that cancer cells can be recovered from peritoneal washings in 35% of cases. These same authors commented upon the astonishing number of cells and tumour clumps in samples of blood taken from the inferior mesenteric vein, thus demonstrating again the inadvisability of unnecessary handling of the tumour until the vascular pedicle has been secured.

Non-Resectable Tumour.

Numerous peritoneal secondary deposits or massive liver metastases indicate a very short life expectancy, and the tumour is best not removed. If the tumour is large and the proximal part of the large bowel distended, a proximal colostomy is required; if the primary tumour is small, this can be avoided.

The tumour may be large and locally fixed, but without evidence of distant metastases; in such circumstances resection should be abandoned only after a thorough trial dissection. Massive resections of adjacent involved viscera are justified provided distant metastases have not occurred. If it is necessary to abandon the attempt to remove the tumour, a proximal colostomy is advisable, because remarkable instances of spontaneous regression and even disappearance of carcinomas of the large bowel have been reported as following proximal colostomy (Ferguson and Black, 1954; Dunphy, 1959).

Daland, Welch and Nathanson (1936) studied 100 untreated patients with carcinoma of the rectum, and the average duration of life was found to be 14 months from the time of the onset of symptoms, with one patient surviving just over four years. In the writer's series the average duration of life has been 11 months.

Palliative Resection.

At operation, a removable tumour may be found, but associated with metastases in the peritoneal cavity or in the liver. A palliative removal is performed if these are not extensive. In the writer's recent series of 186 patients treated since January, 1957, 45 (24%) were subjected to palliative excision.

The sigmoid adhesions are divided. The inferior mesenteric vascular pedicle is ligated opposite the promontory of the sacrum. The sympathetic fibres crossing the iliac vessels are identified and preserved. A layer of fascia covering the sacrum is preserved. If the tumour is above the peritoneal reflection, division of the lateral ligaments may not be necessary; otherwise they are defined, clamped, cut and ligated. When mobilization of the rectum has been completed, a decision is made as to whether it is possible to preserve the sphincters.

Restorative Resection.

Preservation is possible in about half of these cases (22 of 45 in the writer's recent series). Tumours lying 10 cm. from the anus or more can almost always be removed without sacrificing the sphincters. Tumours as low as 6 or 7 cm. from the anus can be similarly treated, because the palliative nature of the operation permits some laxity in the rule that a five-centimetre margin of bowel is necessary below the lower macroscopic edge of the tumour. A final decision concerning restoration must be delayed until mobilization has been completed, because small size of the pelvis, obesity of the patient, or a short mesentery may each interfere technically with the procedure. End-to-end anastomosis is the method of choice, but some form of pull-through operation may be required in very low resections or when pelvic space is restricted.

Permanent Colostomy.

If the tumour is too low to permit restorative procedures, the anus, anal canal and levator ani muscle should be removed. This gives better results than the Hartman type of operation, in which these are left intact. The surgeon moves to the perineum. The anus is closed with strong silk (No. 16, hollow-woven silk), and the perianal, ischio-rectal and levator ani structures are infiltrated with 200 ml. of a 1:200,000 solution of adrenaline in saline. The anus and anal canal are enclosed in an elliptical incision, which is deepened to and through the levator ani muscle. If the abdominal dissection has been completed satisfactorily, no other dissection is required to free the rectum. The perineal skin is closed around a large drain tube, which is led into an underwater drainage bottle or to a continuous suction apparatus. The surgeon returns to the abdominal dissection, and closes the peritoneum snugly in the pelvis. A five-centimetre incision is made in the left iliac fossa and deepened to the peritoneum; which is incised. A bowel clamp passed through the incision is placed across the part of the bowel to be divided. After division, the cut edge of the bowel is subjected to diathermy prior to being withdrawn through the incision. The tumour-bearing bowel must be kept wrapped up until removed from the operation field, because annoying implantation metastases may develop from unexpected local dissemination. The space lateral to the colostomy is closed, and after the main wound has been sutured, the colostomy is completed by interrupted mucosa-skin sutures.

The ovaries should always be removed because of the occasional secondary deposits on them (Stearns, Deddish and Quan, 1959). A loop of small bowel with related mesentery is excised occasionally, and sometimes an adherent caecum has to be removed. Quite commonly it is necessary to resect the uterus and posterior wall of the vagina in continuity with the rectum; but with palliative resections heroic mass excisions should not be considered.

Survival after Palliative Resection.

The average survival after palliative excision of the rectum at St. Mark's Hospital was 1.7 years (Lockhart-

Mummary, 1959). In the writer's series, the average survival after palliative excision was 21 months, measured from the onset of symptoms. One patient with massive glandular metastases survived 47 months (42 months after resection), and another with peritoneal metastases, 36 months (33 months after resection); whilst one patient with a long history of irregular bowel actions with the passage of blood survived 78 months after the removal of a huge tumour.

Radical Resection.

If there is no evidence of spread to the liver or into the peritoneal cavity, the tumour should be treated by radical resection. This is a more formidable procedure, and should not be carried out on patients with poor health. The lesser palliative operation is better tolerated by these, and in any case is probably equally effective. In the writer's recent series of patients treated since January, 1957, 114 of the total 186 (61%) were subjected to radical resection.

After the sigmoid colon has been freed, the inferior mesenteric artery is ligated at its origin from the aorta. The vein deviates from the artery at this level and is ligated separately. The glands to be removed are closely incorporated with these vessels, and as they are stripped distally, the anterior aspect of the aorta is laid bare. It appears unnecessary to remove the glands along the inferior vena cava. Stearns, Deddish and Quan (1959) analysed 122 cases in which the para-aortic and vena caval glands were removed, but in none were malignant foci discovered. High ligation of the inferior mesenteric vessels is also probably unnecessary if the tumour is below the peritoneal reflection. Gilchrist (1959) has only once found an aortic node involved in such circumstances.

The rectum is pushed forward off the sacrum, the surgeon keeping as close to the latter as possible. The lateral wall of the pelvis is cleared of its glands from the common iliac vessels forwards, and from the common and external iliac vessels downwards. This tedious dissection is rewarding in so far as the whole of the lateral ligament of the rectum is removed. The internal iliac artery can be ligated in continuity, but it is not the writer's usual practice. In their own series of 122 cases, Stearns, Deddish and Quan (1959) found 11 patients with these pelvic extramesenteric nodes involved; all but one of these patients had involved mesenteric nodes. If the tumour is above the peritoneal reflection and clear of the middle hemorrhoidal lymph-drainage system, lateral wall dissection is unnecessary, unless there is extensive mesenteric node involvement or the tumour extends deeply (Gilchrist, 1959).

The dissection is carried to the upper surface of the levator ani muscle posteriorly and laterally, and anteriorly as far distally as possible. In the female this extends to the perineal body, and in the male to the apex of the prostate or beyond. Once again, at this stage a decision is made concerning the preservation of the anal sphincters.

Restorative Excision.

If it is possible to remove 5 cm. of bowel and tissue below the lower edge of the carcinoma, if there is enough of the proximal part of the colon, and if there is room in the pelvis, a restorative excision is performed. In the writer's series of 114 radical excisions performed since January, 1957, just over half were restorative (61, or 54%). A clamp is placed across the rectum below the tumour, and the rectum irrigated with 1:500 perchloride of mercury solution. The rectum is divided below the clamp, and the anastomosis performed by a two-layer technique. Although silk is easier to use in the outer layer because it is possible to be more certain of the integrity of the knot, fine chromicized catgut is probably preferable (no. 3/0). At the conclusion of the anastomosis, a drainage tube is placed in the pelvis at the lower end of the abdominal wound. A colostomy or caecostomy is constructed if the anastomosis is under suspicion.

It may be possible to go well below the tumour, with ample colon to reach the rectal stump, but the pelvis

may be too small for abdominal anastomosis. In such cases a "pull-through" anastomosis is performed; this is a popular and successful method in some clinics, but experience is required. The most satisfactory "pull-through" operation entails removal of almost the entire rectum, after which the proximal part of the colon is withdrawn through the anal sphincters. A length of about 10 cm. of colon is left protruding and is trimmed off ten days after operation.

Permanent Colostomy.

If it is not possible to preserve the sphincters, the perineal phase of the operation is completed, and a permanent colostomy constructed in the left iliac fossa. A wide removal of perianal skin and fat appears quite unnecessary unless there is actual involvement of the anal canal by the tumour.

POST-OPERATIVE MANAGEMENT.

After resection, the post-operative management of the patient is similar whether the sphincters have been preserved or a colostomy has been constructed. A nasal gastric tube is not used unless the patients vomit, or unless the abdomen becomes distended. Nothing is permitted to be taken orally until the peristalsis is audible, and this is usually on the second or third day after operation. Penicillin and streptomycin are given for five days. The indwelling bladder catheter is removed when the intravenous administration of fluid is discontinued, usually on the third and fourth days. The perineal tube is shortened on the fourth day and removed on the next, as is the pelvic drainage tube inserted after restorative excision. With the tubes out, the patient is allowed out of bed and by the twelfth or fourteenth day is ready for home.

Patients with a colostomy are supplied with an explanatory booklet. They are given a disposable bag set, and the colostomy is allowed to act naturally without aperients or washouts. The patient should be warned about the initial overactivity of the colostomy, otherwise the irregular discharge so common in the first week and the early part of the second is likely to upset the patient considerably. If this "no-washout" régime proves too difficult for the patient, it is abandoned in favour of daily colostomy lavage.

COMPLICATIONS AFTER EXCISION OF RECTAL CARCINOMA.

Abdomino-perineal excision of the rectum with permanent colostomy is exceptionally well tolerated, and most surgeons engaged in this field can report very low mortality figures. The writer had, at one stage, a consecutive series of 131 cases without loss (Hughes, 1959). Bronchopneumonia and pulmonary embolism may occur, but are uncommon. Occasional slow healing of the perineum is encountered, but this is unusual.

Preservation of the sphincters introduces complications related to the low anastomosis. Pelvic infection tends to loosen the suture line, or alternatively, imperfect suture line leads to pelvic infection. Pelvic infection may cause peritonitis that can prove fatal—a rare complication indeed of abdomino-perineal excision with colostomy. Alternatively, the defect in the suture line is responsible for a faecal fistula; in the male, the fistula communicates with the skin just above the pubis; in the female, the fistula connects usually with the vagina. In the writer's series of 118 restorative excisions for carcinoma of the rectum or recto-sigmoid junction, there have been six complicated by faecal fistulas. Three other patients developed chronic infection above the levator ani, almost certainly caused by a defect in the suture line. This did not lead to further surgery, but nevertheless was an annoying complication.

Bowel function after low anastomosis in the pelvis is imperfect, but adequate. It is common to have diarrhoea with poor control for the first week after surgery, but after this there is steady improvement. No patients have had incontinence of faeces, and none have been disturbed enough to warrant consideration of a colostomy.

After radical removal of the rectum with the pelvic extramesenteric nodes, the sympathetic nerves innervating the bladder are sacrificed, and serious delay in a return of bladder function after operation is the rule. All these patients are sexually impotent.

Suture line recurrence has not been a serious feature of most series of restorative resections published in recent years. There have been no instances in the writer's series so far. It seems certain that routine irrigation with perchloride of mercury is at least partly responsible.

DISCUSSION.

Although a high resectability rate can be achieved in carcinoma of the rectum, it is doubtful whether this is in the best interests of treatment of this condition. Low-grade tumours in the lowest third of the rectum and more advanced carcinomas in elderly patients with a seemingly short span of life to come can often be treated by a relatively minor operation. Furthermore, the expectancy of life with numerous peritoneal metastases or with massive liver involvement is so short that satisfactory palliation is not always achieved by removal of the rectum.

The passage of time will decide whether the more radical removal of the extramesenteric nodes in the pelvis is worthwhile. It doubles the operating time, increases the risk of primary hæmorrhage and commonly results in delayed convalescence because of the bladder dysfunction. Stearns, Deddish and Quan (1959) have cast doubt as to its efficacy in improving results.

It is very difficult to compare and contrast results published in support of abdomino-perineal excision or of restorative excision. Excision can be equally radical in both operations; but the risk is slightly greater with restorative operations in so far as the operation is concerned. This is due to the technical difficulty associated with anastomosis deep in the pelvis. Modifications in the form of the Maunsell-Weir transanal anastomosis and the Bacon-Babcock "pull-through" operations have been introduced; but even these ingenious procedures have not overcome the danger of separation at the suture line.

The impossibility of deciding before operation whether restorative resection can be performed has led to a sharp decline in the number of synchronous combined operations performed by the writer. Also, it is easier to carry out a more complete dissection through the abdomen than through the perineum. If after mobilizing the rectum it is found impossible to save the sphincters, it is a simple matter to complete the removal of the rectum and anal canal. Because an infected hæmatoma is likely to remain above the levator and diaphragm, it is best to avoid the Hartman type of operation.

Recently a review of cases at the Memorial Hospital, New York, showed that preoperative deep X-ray therapy with the 250 kilovolt machine increased the number of five-year survivors in the group with carcinoma of the rectum with involved regional lymph nodes (Stearns, Deddish and Quan, 1959). Operation was performed a month after the course of irradiation treatment. This parallels local experience in the treatment of carcinoma of the cervix. X-ray therapy combined with the administration of 5-fluorouracil is useful for perineal and pelvic recurrence after excision (Crile and Turnbull, personal communication). X-ray therapy has also been combined with vaccine therapy with occasional good results (Graham and Graham, 1959).

SUMMARY.

1. A small number of patients suffering from carcinoma of the rectum are unsuitable for surgery.
2. A pedunculated adenocarcinoma with a pedicle free of tumour can be treated by local excision, provided it is in the lowest third of the rectum where the site of removal can be easily observed later.
3. If laparotomy reveals numerous peritoneal and liver metastases, resection does not always produce as good palliation as do more conservative procedures.

4. Radical resection performed for tumours without evidence of distant spread should include the extramesenteric pelvic lymph nodes if the primary tumour is below the peritoneal reflection. If the tumour is above the peritoneal reflection, these nodes do not require dissection; but the pedicle of the tumour should be secured at the aortic level.

5. Restorative resections can be performed in over 50% of cases of carcinoma of the rectum. A final decision concerning the preservation of the sphincters must be often delayed until dissection in the abdominal cavity has been completed. This is one reason why the synchronous combined excision has been performed less and less frequently by the writer.

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AUSTRALIAN MORTALITY IN THE LATE NINETEENTH CENTURY.

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AUSTRALIA up to the end of the nineteenth century had a relatively small population isolated from other centres, which caused its epidemic history to be quite different from that of settled countries such as England. Pioneering conditions also were responsible for a high incidence of accidental deaths. In this paper, we consider some commentaries on the Australian mortality written before the end of the century, which bring out some of the special features of Australian mortality at that time.

Professor Pell as a Vital Statistician.

Professor M. B. Pell (1827-1879) must be regarded as the most important of the commentators on mortality in Australia before 1900. Born in the United States, Pell was educated in England, becoming Senior Wrangler in 1849 and later a Fellow of St. John's College at Cambridge University. In 1852, he was appointed first professor of mathematics in the University of Sydney. He held this position until 1877, when failing health forced his retirement. Pell was active in many other affairs, and served on commissions on water and sewerage and on Hunter River flood prevention.

The authoritative text of Wolfenden (1954) refers to the standard method of computing mortality rates in childhood from a knowledge of births and deaths as "Pell's method", and cites Pell (1879). Here we can only mention his comments on more general aspects. Pell (1867) notes that New South Wales mortality is much lighter than the English up to the age of 30 years, but at the higher ages the New South Wales mortality is much heavier. He believes that the difference in childhood is due largely to differences in social conditions, especially the absence of poverty in Australia. In other words, in England there were in Pell's time very great differences in mortality between different classes and so between different areas. (William Farr had demonstrated these great variations. Indeed, their presence indicated that much could be done to reduce mortality by improving conditions in the new industrial cities of the north and midlands.) Pell considers first that the excess in the mortality in New South Wales at the higher ages may be due to the keeping alive of the unfit by the favourable mortality at the lower ages, which was quite in line with some contemporary views on social improvements; for, at that time, the views on social amelioration were strongly coloured by Darwin's *Origin of Species*. Pell (1867) later decides that, as many of the older persons have been born in England or Ireland, the explanation is inadequate. He hopes that later studies will be made to decide whether the Australian-born had more favourable mortality than the migrants. Pell (1867) then tabulates the usual functions of the life table based on mortality in New South Wales in 1856-1866.

The second paper of Pell (1878) is a reprint of a series of articles from the *Sydney Morning Herald*. He begins by pointing out that the infant mortality in New South Wales certainly refers to Australian-born persons, and that it is more favourable than the English; from his table there are 106 deaths per thousand births in New South Wales, as against 150 deaths per thousand births in England. Pell (1878) then notices the low infant mortality of the rural areas, and suggests that a dispersal of the Sydney population would be beneficial. He again compares the mortality rates in New South Wales with the English rates, and finds them more favourable up to the age of about 50 years; he notes that it is just in those groups with a high proportion of Australian-born that the advantage chiefly lies, and so he is able to deny that the semi-tropical climate is leading to physical deterioration. He points out that the rate of change in the mortality rates is also extraordinary, for in long-settled countries the mortality rates are as regular "as the planets in their orbits". Pell goes on to show that the advantage of New South Wales lies in the lessened importance of the "zymotic" diseases—that is, the infective diseases—and that variations in incidence of this class of diseases also help to explain the country-rural differences in mortality. He then shows that the high masculinity of the rates in New South Wales is largely due to violent and accidental causes. He concludes his valuable paper with some remarks on migration and the balance of the sexes in the population, and with a criticism of the accuracy of the census returns, especially under the age of five years. Pell's (1879) third paper on these topics may be regarded as a formalization of his remarks in the second, especially his method of computing mortality at ages under five years. Some of his rates have since been used to construct generation rates for Australia (Lancaster, 1959).

Pell (1879) remarks:

The most peculiar feature in our mortality tables is found in the comparative rates for the two sexes. In England, between the ages of 8 and 40, the rates of mortality are greater for females than for males. Here the rates for females are lower than those for males during the whole period of life. In each of the three determinations which I have made, the same thing appears. In 1867 I stated that there was evidently some local cause, increasing the relative death rate of males, or diminishing that of females, during the more active period of life. At one time I was inclined to believe that our climate might be more favourable to women during the child-bearing period of life, than that

of England; but I find that the Medical Profession are, as far as I can learn, unanimously of a contrary opinion. An examination of our accidental death rates sets this question at rest, and proves conclusively that the local cause producing this discrepancy between our rates and those of England, is the much greater liability in this colony of the male sex above the age of 10 to death by accident. The accidents peculiar to this and (I suppose) other newly-settled countries, are met with in riding and driving over almost impassable roads, in attempting to cross swollen and bridgeless rivers, and more than all, perhaps, in reckless riding after cattle through dense forests and scrubs; and the great majority of such accidents occur, of course, to men and boys. The accidental deaths per 1000 of the population above the age of 10 in New South Wales during the years 1860-75, were, for males 2.01, and for females 0.46. In England, for 1870-71, the corresponding rates were 0.99 and 0.23, the colonial rates being thus in excess of the English by 1.02 for males, and by only 0.23 for females.

Other Commentators on Australian Mortality.

A. F. Burrige (1882), an English actuary, made a life table from the deaths recorded in Victoria in 1871 and the census enumeration of the same year. He noted the striking fluctuation in the crude death rate in Victoria over the years 1871 to 1880. Usually it ranged from 13.5 to 15.8 per thousand, but in 1875 it was 19.5 per thousand *per annum*. (Tables of the crude death rates for the Australian colonies can be obtained conveniently from the tables of *Demography*, the annual bulletin of the Bureau of Census and Statistics, Canberra, for the years 1957 and 1911.) For easy reference I give the crude death rates by year in Victoria and in New South Wales in Figure 1. Large variations in mortality in the earlier years are evident. With the passing of the higher mortality from infective diseases, the curve has recently become smoother. In the more recent years since 1900, only the influenza epidemic of 1919 has been sufficiently large to cause any marked rise in the crude death rates. However, the percentage disturbances caused by measles in 1860, 1866 and 1875 (associated in the last-mentioned year with an epidemic of scarlatina) were greater than that caused by influenza in 1919. We may note that in Victoria there were 985 deaths from scarlatina and 1541 deaths from measles in 1875, and in the next year 2240 from scarlatina and 5 from measles. In his later article, Burrige (1884) recognizes that there are very great changes in the incidence of the infectious diseases from year to year in Australia. He discusses deaths by cause briefly, and rejects a popular theory that deaths from phthisis were due to the migration of invalids from England. He shows that almost 93% of such deaths from phthisis were those of persons who had lived for more than five years in Australasia. Burrige (1884) finally concludes:

Among the circumstances producing a low rate of mortality must be reckoned the sparseness of the population; the small proportion of old lives; and the absence of that large class of persons the mortality amongst whom is increased by a difficulty in obtaining the necessities of life . . . Immigrants are for the most part, healthy and robust persons; and this system of artificial selection, therefore, operates in reducing the death rate.

These rapid fluctuations in mortality are closely associated with the smallness of the population in Australia, particularly in the earlier years. I have discussed this point in my paper on measles (Lancaster, 1952), where a table is given for the years 1890 to 1949. In Table I of that paper are given the deaths, where available, from measles for the years 1860 to 1889 in the colonies. In some colonies, years of violent epidemics are followed by years in which there are no deaths. In the years immediately before 1866, measles appear to have been endemic in Victoria, but not in the other colonies; in 1866 there was an epidemic in Victoria followed by epidemics in South Australia and New South Wales (figures available only for the city of Sydney) in 1867. There were no deaths from measles in Western Australia at the time of the 1866-1867 and 1875-1876 epidemics in the eastern colonies, and indeed no deaths between 1862 and

1880. Presumably this means that there were no measles in Western Australia over these eighteen years, reflecting the protection afforded by the long sea voyage from England and the small traffic from the eastern colonies.

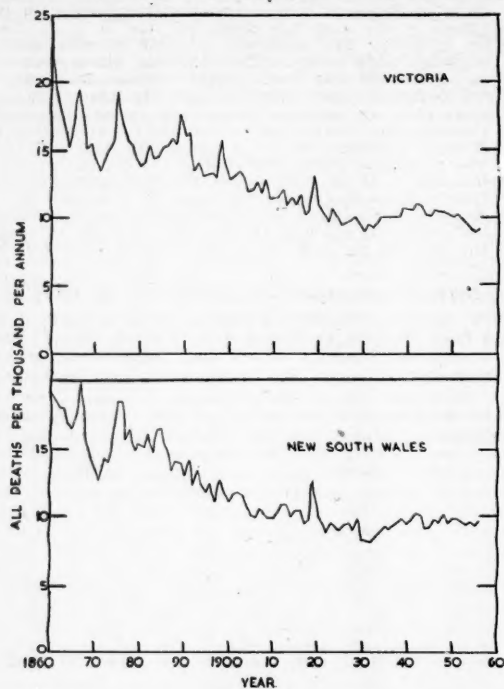


FIGURE I.

The crude death rate in Victoria and in New South Wales, 1860 to 1957.

Figure II shows the deaths from measles in Victoria and in New South Wales for each year from 1860 up to the present time, and illustrates the wide fluctuations in the

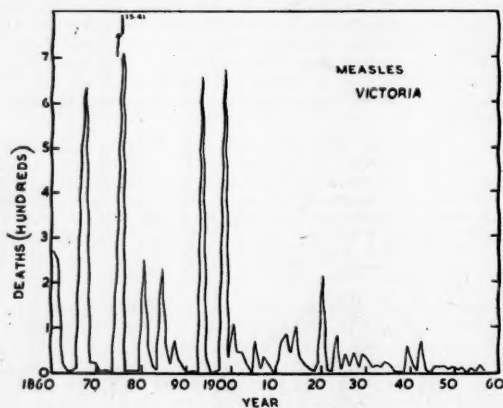


FIGURE II.

Deaths in Victoria from measles, 1860 to 1957.

number of deaths by year. When the number of deaths is high in two consecutive years, this is often due to an epidemic continuing through the summer, and so if the deaths were taken for smaller intervals, the relative or percentage fluctuations would be even greater. This picture of irregularly-spaced epidemics may be compared with the two-year cycle, which has been characteristic of the experience of many English cities. The two-year

cycle is usually explained (e.g. Stocks, 1942) by the fact that infants do not move about very much between family groups or isolates. The toddlers are the chief disseminators of the disease under intensely endemic (English) conditions, since most older children have already had the disease. In one year the infants and

TABLE I.

The Deaths from Measles in Australia by Colony and Year and Deaths from Scarlatina in Victoria by Year.

Year.	Deaths from Measles.						Deaths from Scarlatina.
	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Victoria.
1860	348	274	—	1	0	—	—
1861	46	252	—	111	48	—	871
1862	4	20	—	104	0	—	393
1863	—	8	—	0	0	—	312
1864	—	7	—	0	0	—	278
1865	1	11	—	0	0	—	215
1866	0	427	—	0	0	—	462
1867	462	630	—	112	0	—	621
1868	1	24	—	17	0	0	460
1869	2	24	—	0	0	0	224
1870	0	3	—	1	0	0	24
1871	0	4	—	0	0	2	27
1872	1	7	—	0	0	1	185
1873	0	1	—	1	0	0	188
1874	62	256	1	280	0	0	121
1875	762	1541	178	75	0	129	985
1876	35	5	33	5	0	1	2240
1877	2	6	1	1	0	2	183
1878	1	5	1	2	0	0	136
1879	3	3	1	1	0	0	61
1880	270	252	0	9	1	0	26
1881	88	62	3	72	0	45	86
1882	10	15	32	11	0	0	89
1883	47	7	59	12	30	0	59
1884	45	233	6	139	95	1	34
1885	10	69	2	6	4	20	14
1886	6	20	1	3	0	1	14
1887	52	78	0	2	0	0	4
1888	218	30	3	1	0	0	21
1889	13	19	0	1	0	0	41

¹ A dash indicates that the number is unavailable.

² Deaths for the metropolis only.

³ In the four years 1861 to 1864 the deaths in Victoria from diphtheria were 510, 360, 331 and 451 respectively.

toddlers have the disease, and in the next there will be fresh susceptibles, the new infants, but not enough susceptible toddlers to be effective in disseminating the disease freely from family to family. In this second year, there are thus few cases. In the following year both infants and toddlers will be susceptible, and conditions are ripe for another epidemic. The fluctuations caused in total mortality were not so marked under these "English" conditions as they were under the "Australian" conditions, because the disease tended to affect only one age group in England. Further, English cities would not be all in the same phase, some having their epidemics in odd years and others in even years, and this has an averaging-out effect on the total deaths from all England. Figure III shows the regular fluctuation in the annual number of deaths from measles in London.

Other actuaries were also interested in establishing whether the mortality rates in Australia or for Australians were similar to those holding for the English population. Bremner (1889) compared the rates for the Australasian colonies and found the lightest rates in New Zealand, where the mortality rates at ages under five years were less than half the corresponding English rates. He noted the large urban-rural differential in mortality in Australia, and blamed typhoid fever especially for it.

Dovey (1893) noted that the death rates were in a state of flux, and that it was necessary constantly to review whether the tables used by the actuaries were realistic. He commented that Pell's method would give a mortality rate at ages under five years slightly too high because of migration of young children. He was greatly concerned with the urban-rural differential in infant

mortality rates, and gave figures to show that it was due to infective disease, especially gastro-enteritis. He also was impressed by the especially favourable death rates of females at the higher ages.

Duckworth (1894) gave life tables on the experience of 1881 to 1890 and discussed some of the economic and demographic implications of population growth.

Some special investigations on the mortality of select lives were made by officers of the Australian Mutual Provident Society (Black, 1882; Teece, 1891, 1891-1892, 1893 and 1911), and by the consultant actuary, G. King (1920, 1921 and 1924); but their value is greatly lessened by the inclusion at, say, age 24 years, not only of persons aged 24 years, but also of those aged 23 "weighted" one year and those aged 22 years "weighted" two years.

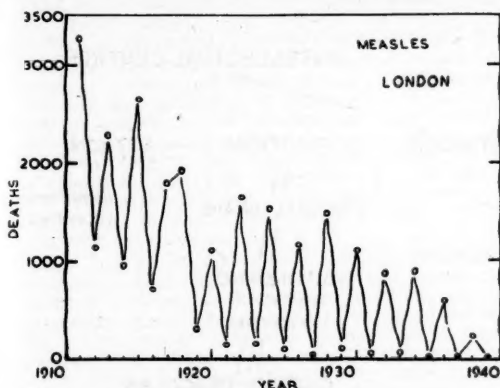


FIGURE III.

Deaths in London from measles, 1911 to 1940.

Other investigations on the mortality of special groups have been reported by Moors and Day (1901), by Smith (1906), by Thodey (1929), by Gouge (1909) and by Trivett (1910, cited by Knibbs, 1917), and more detailed references are given to their life tables in Knibbs (1917) and Wickens (1930).

C. H. Wickens (1930) discussed Australian life tables and mortality, and noted the high accident rate under pioneering conditions and the relative maximum of the death-rate of some generations in young adult life. However, Wickens really belongs to a later period than the others. It may be noted here, in passing, that many of the admirable features of the *Report of the Statistician on the Australian Census of 1911*, which was cited above as Knibbs (1917), were due to Wickens, who was Supervisor of Census at that time.

Conclusions.

Colonization in Australia in a hot climate led to unexpected epidemiological results. There was not in Australia any large settled native population with endemic diseases such as malaria at the time of the first colonization. The aborigines were nomadic, and there was little or no spread of disease from them to the European settlers. Because of the great distances from other population aggregates, Australia remained free of some infectious diseases for many years. The isolation and the small population size led to violent epidemics, of measles in particular, at irregular intervals, which contrasted with the rather regular behaviour of such diseases in England. The early commentators were not prepared for this altered behaviour of the infectious diseases in a country with a population not large enough to sustain continued epidemics, and we have seen how both Pell (1878) and Burridge (1882), were at first unwilling to give infections as the cause of the fluctuations in the crude death rate. However, many commentators since Pell and Burridge have also failed to appreciate the importance of the infectious diseases in the recent

reductions in mortality. Accidents under pioneering conditions were an important class of cause of death.

Acknowledgements.

Thanks are due to Dr. H. F. Bell and Miss M. Anderson, of the Australian Mutual Provident Society, for some information on Professor Pell.

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THE CIVILIZED PATTERN OF HUMAN ACTIVITY AND CORONARY HEART DISEASE.¹

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ISCHEMIC HEART DISEASE is the final stage of a process in which the continually varying metabolic requirements of the myocardium are not met by the coronary blood supply. Such a deficiency can be due to mechanical

¹Read at the annual meeting of the Cardiac Society of Australia and New Zealand on May 25, 1959, at Adelaide.

obstruction; but from many studies it appears that coronary atheroma is not necessarily related to the degree of ischaemia; narrowing and occlusion are only partly related to it (Morris and Crawford, 1958). This means that, apart from the static anatomical factor, there must be in many cases some disturbance in the dynamic adjustment of the coronary circulation to the myocardial needs. We shall term this dynamic adjustment cardio-coronary homeostasis. It can be represented by the relationship myocardial needs:coronary blood supply, which has to remain constant.

It is worth stating here that "myocardial needs", which are directly related to the amount of blood to be propelled, can be reduced by cardiac muscle or vasomotor changes (as, for instance, by increase in myocardial tone or by blood redistribution). This means that general cardio-vascular adaptation is part of cardio-coronary homeostasis.

The major demands on cardio-vascular performance come from neuro-muscular activity. It is during this activity that the homeostatic mechanism of cardio-vascular and coronary adjustment goes into action and has to be at its maximum efficiency. The ischaemic phenomena may not occur during neuro-muscular activity; but nevertheless this activity is a major factor in the blood supply: myocardial needs relationship. It may strain such a relationship; it may also result in the establishment of a favourable working mechanism.

Because the anatomical factors are not always related to the increasing incidence of ischaemic heart disease, it is plausible to assume that some factors in the western way of life impair, prevent or delay the homeostatic adjustment of the cardio-coronary system to neuro-muscular activity.

Although some aspects of such adjustment are not yet elucidated, it is known that many factors are involved; some act mechanically—as, for instance, in the increase of cardiac output through augmented venous filling and greater stretch of the heart muscle fibre; some start by acting chemically (as the rising carbon dioxide tension on cardiac centres). Such factors are constant or obligatory and appear at a definite stage of any neuro-muscular activity; they do not operate before or at the beginning of such activity. The adaptation of the coronary system follows even later on.

On the other hand, we know of the regulation through the autonomic nervous system, with its multiple reflexes and pathways including hormonal activity. This system can exercise a simultaneous influence on the activity of the heart itself and on the coronary vessels; it would be therefore of major importance in prompt cardio-coronary homeostasis. Some of these mechanisms for cardiac adaptation act through reflexes (such as the Bainbridge reflex) and are also of a constant nature; but as a whole the autonomic nervous system is under the influence of higher centres such as the thalamus, the hypothalamus and their various connexions. It is at this level that the adaptation of the cardio-vascular and coronary system gets a booster effect, over and above the autonomic adjustment to the demands of the work required.

The diagram in Figure 1 is meant to show the group of factors promoting cardio-vascular and coronary homeostasis. The neuro-muscular activity *per se* induces such adaptation by mechanical factors (interrupted line) or through the autonomic nervous system by reflex activity (dotted line). These are the constant or obligatory factors. On the other side of the diagram are shown the variable factors—the activation or stimulation of the autonomic nervous system produced by the centres grouped here as the "visceral brain" (rhinencephalon, hypothalamus, cerebral reticular formation). Such centres control the affective behaviour and translate the emotions into somatic repercussions. The stimulus as shown in this diagram may or may not have an emotional charge. When it is emotionally charged, it will affect the variable factors by initiating certain patterns of autonomic nervous and hormonal activity.

Whilst our biological system has changed little in the course of the last centuries, the world around us has.

This means that stimuli may be different; but an even more important fact is that, with our more discriminating and intellectual behaviour, we select different stimuli as signals for action (we cross the intersection, not when the road is clear, but when the green light appears).

I have stated that the reaction of the autonomic nervous system depends on the stimuli and is the only variable factor in cardio-vascular homeostasis. It is logical to postulate that this variable factor is the one related to the deficient cardio-coronary adaptation and to the prevalence of ischaemic heart disease in civilized society. The main problem, then, is the behaviour of the autonomic nervous system in conditions of civilized activity. Prior to discussing this, I shall quote succinctly a few examples of the way in which the variable participation of the autonomic nervous system influences cardio-vascular and coronary homeostasis.

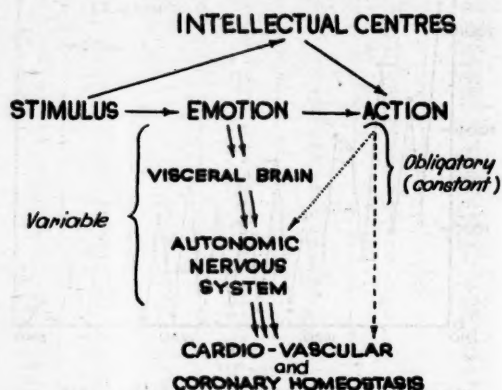


FIGURE 1.

S. Wright (1956) stated that emotional states affect cardiac and vasomotor centres. P. Wood (1956) noted that the strength of cardiac contraction varies with sympathetic tone, and that increased adrenergic activity may be regarded as the first cardiac reserve. Cavert (1958) demonstrated protective effects of catecholamines against noxious agents (such as carbon dioxide, acidosis, etc.). Matthes (1957) observed that autonomic nervous system stimulation promoted cardiac adaptation prior to neuro-muscular activity. Donald Gregg (1958) stated that coronary flow depended on (i) smooth muscle tone in coronaries, and (ii) ventricular contractility, both at least partly controlled by sympathetic tone. Arnulf and Chacornac (1957) proved that stellate ganglion stimulation increased coronary flow, which could be further augmented by adrenaline. L. Katz (1957) observed that in the emergency "shift-in-gear" mechanism of cardiac adaptation, catecholamines increased coronary flow. According to W. S. Hoffman (1955), adrenaline production increases in blood the fibrinolysin level.

The part played by autonomic innervation and the related hormones in the blood distribution is so well known as not to require emphasis. Such distribution is one of the factors of cardio-vascular adaptation to activity.

Once we accept that the autonomic nervous system and its hormonal extensions contribute to the economical running of the myocardium and also take part in regulating the coronary blood supply, we can understand that the deficient participation of such a system can affect either or both the factors of the relationship (myocardial needs:coronary blood supply) and lead to minor or major disproportion, with resulting ischaemic phenomena.

¹Grace and Graham (1952) suggest that emotion can be defined as attitude with its associated physiological changes.

The degree of activity of the autonomic nervous system is related to emotional tone and emotional states.¹ I suggest that this relationship is of physiological advantage; necessary resources, such as those of the cardio-vascular and coronary system (including maybe "shift in gears"), can be mobilized before neuro-muscular action starts, when the stimulus for action is also an emotional one. An internal *milieu* favourable to action is created before the cerebral order for it has to be executed. It is logical to assume that in such conditions homeostasis is at its maximum efficiency.

Such homeostatic mechanisms were probably established at a primitive evolutionary stage of human history. At this stage, action or activity either was reflex, or followed a direct external or internal stimulus capable of producing emotional charge—as, for example, in the case of hunger, sexual desire, fear or the necessity for fight or flight. In other words, the emotional element leads to presumably appropriate reactions, maintaining the cardio-vascular and coronary homeostasis during activity or preparing favourable conditions for it.

Now we shall consider the prevailing pattern of neuro-muscular activity in Western society; our main preoccupation will be the degree of integration of the autonomic nervous system in this "civilized pattern of activity". We have already seen that this integration can be related to emotional factors; but other factors—such, for example, as conditioning or type of activity—can be also brought into play. In habitual tasks the autonomic nervous system is promptly integrated because of previous recurrent conditioning.

The pattern of activity of the Western man differs profoundly from the pattern of the primitive man. In civilized society, most of our activities are not the immediate result of an external or emotional stimulus. We act and we are taught to act on cerebral orders only. By the time when an action is being performed, the initial motive has been intellectually elaborated and has long since lost its emotional or physical impact. Civilized man acts or performs according to a programme marked out weeks, months or years beforehand. Even if we adjust our actions to a change of circumstances, we do not do it spontaneously; we follow a set of intellectual and planned rulings, dissociated from what our reflexes, emotions or wants may be at the moment of action.

This dissociation between stimulus, emotion and action has been regarded for years as typical of civilized man. In accordance with Canon's observation on the biological reaction of fight or flight, it has been postulated that many organic diseases are due to the rational inhibition of emotionally prepared actions.

We have, then, emotion without action; but the counterpart of it, which I stress—action without emotion—is equally typical of civilized behaviour and activity.

It is obvious that we now present our organism with a situation without precedent in the biological past—that is, dissociation between emotional charge and action. The autonomic nervous system lacks one of its stimuli to adjust the internal economy to external activities. Such adjustment is now delayed, and appears only as a result of metabolic or other changes during activity.

If we analyse the impulse initiating any organized neuro-muscular activity, we shall realize that this impulse may derive from (i) an emotional stimulus (fleeing from fire), (ii) a habit or conditioning (walking to work after breakfast) or (iii) intellectual decision (training for future Olympic Games). These factors may overlap, favour or inhibit each other; but in civilized conditions the intellectual choice is the one we are taught to adhere to at the expense of others; this typifies the Western civilized man.

I presume that in psychological language "intellectual choice" as the impulse to action would correspond to "secondary" or "tertiary", or to a "high order of motivation". I would suggest that in this case the impulse to action, instead of being a direct response to a stimulus, is based on intellectual appreciation of the situation in

the light of past experience and learning, and with a long-term view to the future.

I would state, therefore, that of the three impulses (emotion, habit and intellectual choice) the last has the weakest connexion with the autonomic nervous system. I shall postulate that, because of the imposed cultural rulings, the civilized pattern of activity is characterized (a) by long-term motivation with a long-term programme, (b) by regulation of current activities by intellectual choice, (c) by inhibition of the emotional reactivity during action unless it happens to favour the immediate task. This means that the emotional attitude to the activity itself may be negative or positive, but mostly will be neutral.

The equality of opportunities typical of democratic countries favours both the self-reliance of the individual and his conviction that his present and future status depends mostly on his performance, endurance, perseverance and long-term planning. This is especially true for the wealthier countries, where the possibility of advancement is at least theoretically unlimited. Things were different in the not distant past, when class distinctions put a limit to many ambitions and would discourage hard self-driving. Another characteristic of democratic countries is the reliance on the sense of responsibility of the individual in attending to his job, with no threat of immediate reprisal in case of default. Such a threat (unfortunate as it may seem) is an adequate emotional stimulus. A crack of the whip is probably a good adrenergic agent.

Many occupational activities of today do not favour interplay between the autonomic nervous system and cardio-vascular adaptation.

With the advent of automation, even the activity of the ordinary workman ceases to be a routine succession of movements, but follows intellectual judgement on the next step to be taken. This replacement of routine by intellectual guidance prevents the automatic triggering of the autonomic nervous system by conditioning during recurrent activity.

Because the finished product is the result of the activities of many individuals, there is no rewarding feeling of creative achievement. Even if there is a spirit of competition, there is usually no actual emulation at work (as, for example, in log-chopping competitions); the judging is deferred and based on final results (for example, six-monthly or yearly between salesmen of the same company). The introduction of hire-purchase buying reduced the "target excitement", which can be an incentive to extra work or extra effort. The stimulating desire for possession or the sense of want is satisfied immediately. The reason for extra effort is then only the knowledge of the impending payment time.

It has to be emphasized also that some occupations or callings imply frequent changes or burst of activity, and because of that impose sudden demands on the cardio-vascular system. Such occupations or situations always existed—as, for example, in maternal duties with many children, in action on battlefield, or in case of aggression from the outside world. All this can still occur in modern society. In these examples there is an emotional urgency; the activity to be undertaken is heralded by a strong emotional stimulus which prompts the autonomic nervous system into action. Similar requirements of rapid change or bursts of activity occur frequently in some civilized professions; the general practitioner is an obvious example, the business executive is another. But in their case the stimulus for activity is not an emotional one—it is a conventional signal like a telephone call or stock exchange report; the action follows an intellectual elaboration; there is no emotional upheaval to set the whole body in physiological readiness for action.

My point is that the so-called stressful situations requiring action vary considerably in their emotional content. The stress of a doctor called out repeatedly at night is different from the stress of a mother who has to attend to her acutely ill child. In the case of the doctor the impulse to action is intellectual; he knows it

is within his duties. In the case of the mother, she feels she has to act. As we know, the difference between "knowing" and "feeling" is that in the former one is guided by his neo-cortex (which is the centre for intellectual activities) and in the latter there is a major participation of the visceral brain which controls the affective behaviour (McLean). It is obvious that the "feeling", or the emotional factor, is the one which will lead to mobilization of the autonomic nervous system; it will help the mother but not the doctor.

It is difficult to state whether there are more emergency situations calling for action in the present than in the past societies; but it is quite clear that in Western civilized society the integration of the autonomic nervous system into neuro-muscular activity in such situations often lacks the backing of emotional stimulus.

Recent studies (Thorn *et alii*, 1956; Connell *et alii*, 1958) have demonstrated adreno-cortical and possibly adreno-medullary activation under influence of strong emotional factors preceding or accompanying severe muscular exercise (for example, competitive boat racing); but one would like to have more experimental evidence of increased hormonal or autonomic nervous system activity during ordinary physical exertion. This so far can be presumed only from everyday and commonplace observation.

We all know that emotional or psychological factors serve to enhance performance or productivity, increase feeling or zest, or lessen subjective fatigue—as, for example, in team activities, in having music while walking or marching, in any even minor competitive activity. There is an obvious and effective emotional stimulus in a game of squash raquets against an opponent, as compared to hitting a ball in individual training.

The importance of emotional tone in purposeful neuro-muscular activity has been well acknowledged in human experience, and is often used for practical purposes. The "pep talk", which makes use of incitement or threat, the realistic visualization of an aim, an immediate reward or incentive payment, are well known examples of an emotional stimulus of which the obvious target is integration of the autonomic nervous system into the body activity.

I have so far tried to demonstrate that adaptation of the cardio-vascular and coronary system is impaired in the conditions of civilized society. I am not attempting yet to define whether this impairment acts mostly as a predisposing or precipitating factor, or whether it is the summation of recurrent maladaptations that eventually leads to the ischemic phenomena. My point is that the specific physiological pattern of cardio-coronary homeostasis is disturbed because of our "unnatural" conditions of activity; most probably many factors act or fail at different stages of development of ischemic heart disease. My main emphasis being the homeostatic factor in ischemic heart disease, I have disregarded without denying the possible dietetic, age, familial and other factors influencing the coronary anatomy.

In order to confirm my speculative hypothesis, a specific study would be required: one would have to demonstrate that characteristics of the civilized mode of activity appear more frequently amongst persons suffering from ischemic heart disease.

So far the problem has not been put that way. The question of emotion and cardio-vascular physiology has been mostly considered in relation to anxiety and tension, when emotions, conflicting or suppressed, appear to be detrimental because of unnecessary readiness of a system or because of possible inhibitory influences on the autonomic nervous pattern. I maintain that emotional stimulus in primitive or natural situations is an adequate stimulus for both neuro-muscular activity and cardio-vascular adaptation.

It should be noted that emotional stimulus does not mean any or every emotion; the autonomic nervous pattern varies with diverse emotional states. I suggest that emotional stimulus for action is related to basic

motivational drives, and differs from these only quantitatively. We know now that in these drives there is enhancement of activity with alertness of the organism; through the reticular facilitatory system (mesencephalic and bulbar reticular formation), a "high state of physiological efficiency is achieved". There is not only increased reaction, but also highly adapted response. This activation controls cortical tone, muscular activity, sympathetic tone (Dell, 1958; Head, 1926; Magoun, 1950; Moruzzi, 1949).

There have been some studies on the "coronary personality" (Dunbar, 1936; Miles, 1954). The results were not conclusive; but in most of them only "fundamental" traits were studied, and an effort was made to discard the cultural influences or the superimposed pattern due to profession or situation (Forsman and Lindegard, 1958). This means that the acquired civilized characteristics have been missed or omitted.

If a study is to be made of the influence of the civilized pattern of activity on coronary heart disease, the emphasis should not be so much on the constitutional psychological personality or temperament as on acquired behaviour and mode of action, self-imposed or socio-economically imposed by the "civilized" conditions.

One of my premises has been that such "civilized" conditions, and not the relatively unchangeable psychological or physical constitution are the cause of the increasing incidence of coronary heart disease. What will have to be demonstrated is that the "typical Western man" (as presented in the following tabulation) predominates amongst coronary patients, especially when they are engaged in occupations implying frequent changes of activity with no emotional stimulus.

The Typical Western Man.

1. He has a broad time prospective and strong orientation to the future.
2. He seems to be self-directed and self-disciplined.
3. He is detached from strong desires for immediate gratification.
4. He selects activities for potential achievements, not for the pleasure of work itself.
5. Although in every choice there must be an emotional element, once this choice is made, further emotional influences are subordinated to rationally patterned behaviour.
6. He has a conscious awareness of responsibility and is rarely motivated by actual enthusiasm.
7. He is reliable. When necessary, he drives himself to work through rational self-imposition.

Summary.

Because cardio-vascular performance is closely related to neuro-muscular activity, it is worth inquiring whether some patterns of this activity may not be a factor in cardiac morbidity.

The cardio-vascular adaptations to neuro-muscular activity constitute a fundamental homeostatic mechanism established in biological antiquity. Many links in the mechanism are controlled by the autonomic nervous system (blood redistribution, vasomotor and myocardial tone, etc.). The coronary adjustment to myocardial needs is a part of this mechanism.

In the relationship myocardial needs: coronary blood supply, deficient adaptation can affect either or both factors and lead to ischemic phenomena.

The civilized Western man, who appears to be more prone to coronary heart disease than his primitive ancestor, has also adopted a different pattern of activity. Because of Western cultural teachings and modes of behaviour, there is dissociation between stimulus, emotion and action. We are all aware of the emotion without action which can cause symptoms of disease.

I am now stressing the action without emotion; equally typical of the Western man, it implies that most of our activities are cerebrally planned. Because of lack of immediate emotional stimulus, there is less integration of the autonomic nervous system into the body activity;

there is less efficient cardio-vascular and coronary adaptation. This maladaptation, either by frequent recurrence or in combination with anatomical factors (coronary narrowing), may lead to ischaemic phenomena.

Conclusions.

1. How a man works and his attitude to work may be a factor in the increased incidence of ischaemic heart disease.
2. The integration of the autonomic nervous system in neuro-muscular activity may be deficient in Western society.
3. The deficiency is probably caused by a rationally imposed behaviour and mode of work.
4. In a future study on the influence of civilized patterns of activity on coronary heart disease, the emphasis should not be so much on the constitutional psychological personality as on the acquired behaviour and mode of activity, self-imposed or socio-economically imposed by Western civilization.

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PREGNANCY AND DIABETES INSIPIDUS.

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THE association of pregnancy and diabetes insipidus is very uncommon. Bleakley noted that up to 1933 only 25 such cases had been recorded, and Hendricks, in a later review in 1954, considered that less than 50 cases had been formally published up to that time. Furthermore, in some of these cases the diagnosis would not be regarded as established by present-day methods. Blotner and Kunkel (1942) reported three cases occurring in 50,000 deliveries at the Boston Lying-In Hospital, and concluded that the incidence of the disease was similar to that in the population at large—that is, about 1:15,000. It is on account of its rarity that most of the reports concern individual cases. Although our knowledge of the endocrine function of the neurohypophysis and the relation of this gland to the hypothalamus has been considerably clarified in recent years, there are still gaps in our understanding of the physiology and pathology of this unique system. In the present report, the progress of pregnancy in a patient with diabetes insipidus of the inherited type is described.

Report of a Case.

Mrs. A., a primigravida, aged 19 years, presented on November 14, 1957. Her last normal menstrual period had been on August 21. She said that she had been excessively thirsty for as long as she could remember, and had been receiving pituitary injections for the past 12 years, diabetes insipidus having been diagnosed at the start of this latter period. Prior to her becoming pregnant, injections of 1 ml. of pitressin tannate had been necessary every two or three days, and there had been no change in this dosage during the early months of the pregnancy. On questioning of the patient, it was evident that there existed a strong family history of the disease. Her father and four other relatives all ingested excessive amounts of fluid. Apart from some morning sickness over the previous two weeks, the patient said that her general health was excellent.

On examination, she was noted to be 4 ft. 11.5 in. in height, and weighed 177 lb. Her blood pressure was 120/70 mm. of mercury. General examination, including the central nervous system, revealed no abnormality. The uterus corresponded in size to an 8 to 10 weeks' pregnancy. Her haemoglobin value was 12 grammes per 100 ml., her blood group was O, Rh-negative, and the Kline test produced a negative response.

One month after her initial visit, she was admitted to hospital with hyperemesis gravidarum, which had not responded to the usual measures, including antiemetic drugs. There had also been a slight vaginal loss of blood for two days previously. However, in hospital she settled down very quickly, and she was discharged five days later.

On December 26, she again presented with some nausea and vomiting, but in addition she was having mild uterine contractions every six minutes accompanied by a constant suprapubic ache. This had followed her pituitrin injection given that morning. On examination of the patient, the cervical os was noted to be closed with the mucus plug *in situ*. Some contractions were palpated in the uterus, but after she had been observed for about three hours they were noted only very occasionally. On January 19 she was examined in the emergency department, having fainted after her pitressin injection. She complained of sharp lower abdominal and back pain. As only mild and infrequent contractions were observed, she was reassured. The patient said that she had occasionally experienced somewhat similar colicky pains after injections prior to her pregnancy.

On March 3, 1958, she was admitted to hospital complaining of severe uterine cramps following the pitressin injections, and also of generalized muscular aches and pains, particularly in the limbs. Her general condition was satisfactory. In view of the history it was considered that she might be depleted in salt, and accordingly she was given 5 grammes of sodium chloride orally three times a day, and her serum electrolyte levels were determined the following morning. These values, in milliequivalents per litre, were: sodium, 140; chloride, 107; potassium, 3.8. Table I shows the effect of the salt ingestion on the output of electrolytes

in the urine over the next four days. In addition to the appearance of increased amounts of sodium and chloride in the urine, there was also a significant increase in potassium which returned to a normal level three days later. Her general condition soon returned to normal.

Her subsequent preconfinement progress was satisfactory, apart from two further hospital admissions for threatened abortion due to uterine cramps. This increase in uterine sensitivity to the pitressin unfortunately corresponded to the time when increased amounts of the drug were required to control the diabetes. In view of this, she was advised to administer the major part of the injection subcutaneously instead of intramuscularly, in an endeavour to obtain a more even absorption. In Figure I the urinary levels of electrolytes and the specific gravity of the urine are shown graphically for each twelve-hour period over four days. The marked diminution in fluid output, with elevation of the urinary specific gravity, is apparent in the 36 hours after the injection of pitressin. In addition, the total electrolyte content in the urine was seen to fall over the same period. A Hare test performed during this period in

increased salt intake on March 3, and then on the day after delivery. The chloride and potassium levels are comparable with those of sodium, with the exception that both are reduced in the early puerperium. The reason for this, especially in the case of the chloride ion, is not clear. The increased 24-hour urinary output in the first two days of the puerperium is probably related more to the physiological diuresis occurring at this time than to insensitivity toward the administered hormone.

Discussion.

Owing to the rarity with which pregnancy is associated with diabetes insipidus, the opportunity for the study of such cases is very limited. Of the cases recorded in the literature up to the time of Hendrick's report in 1954, the majority were concerned solely with clinical aspects of the disease. It is only very recently that satisfactory techniques for the assay of the posterior pituitary lobe hormones have been described (van Dyke *et alii*, 1955).

With regard to the behaviour of the disease during pregnancy, there seems in the majority of cases to be some aggravation, with greater difficulty in the control

TABLE I.
The Effect of Ingestion of Sodium Chloride Tablets on the Urinary Excretion of Sodium, Potassium and Chloride.

Date (1958).	Sodium Chloride Administered. (Grammes.)	Urinary Electrolytes. (Grammes per Day.)		
		Na ⁺ .	K ⁺ .	Cl ⁻ .
March 3	15	9.45	9.30	7.21
March 4	5	5.70	9.25	9.54
March 5	—	3.88	10.0	10.1
March 6	—	2.6	2.3	2.66

hospital produced the type of response expected with diabetes insipidus, with increase rather than reduction in urinary output following the intravenous infusion of hypertonic saline.

Up to the time of her labour, which commenced on June 30, she had evidenced no oedema, and her weight gain and blood pressure had remained within normal limits. When she was examined at 1 p.m. on the day of her admission to hospital she had been in labour for four hours. Contractions were occurring every five minutes, and were of moderate severity. The fetal head was well into the pelvic brim, although not engaged. The cervix was half an inch long and the os was dilated to admit three fingers. Over the ensuing 24 hours, strong contractions occurred with very slow cervical dilatation. A lateral X-ray film of the pelvis with the patient erect showed that the normal-sized fetal head was well engaged in the occipito-transverse position. Accordingly, continuous extradural anaesthesia was commenced, with immediate relief to the patient. Good contractions continued, and the infant was delivered with the aid of forceps six hours later. Just prior to delivery, meconium staining of the liquor had been observed. The third stage was completed with the aid of 0.5 mg. of ergometrine given intravenously. The blood loss during the third stage was 8 oz. The infant was a male and weighed 8 lb. 7 oz. His condition at birth was fair, breathing being fully established after five minutes.

The subsequent progress of the baby was satisfactory. The condition of the mother, with regard to the diabetes insipidus, improved after delivery. Pitressin was necessary only each second or third day, as had been the case prior to the commencement of the pregnancy. Breast feeding was established satisfactorily, and the infant was gaining weight on discharge from hospital 10 days after delivery. However, when the patient was examined four weeks later, she said that her milk had diminished considerably in the second week after she left hospital and that the infant was now artificially fed. Although she was questioned on the presence of a draught or let-down reflex, it could not be elicited from the patient that this had occurred. Involution of the organs of the generative tract had proceeded normally. The baby did not seem to be unduly thirsty, and by five weeks was not needing to be fed in the period 10 p.m. to 6 a.m.

Table II gives the values of the urinary and serum electrolytes during the pregnancy, labour and puerperium of this patient. The usual dose of pitressin needed is also shown in the table. It can be seen that the values for sodium in the serum are normal throughout, with increased values in the urine observed on two occasions—after

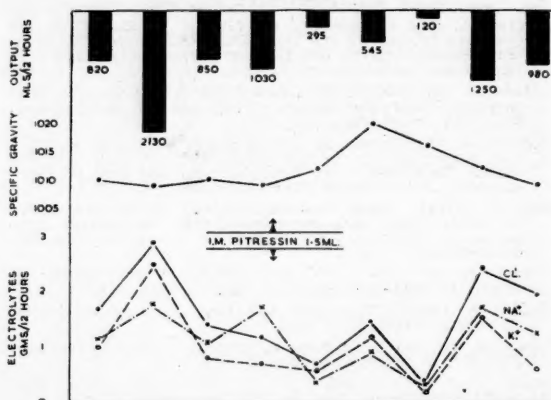


FIGURE I.
Urinary electrolyte content, and output and specific gravity of urine before and after intramuscular injections of pitressin.

of polyuria and thirst, even with increased amounts of antidiuretic hormone. According to Blotner and Kunkel (1942), the commonest form of association of the two conditions is a transient appearance of the disease during pregnancy, particularly in the latter months. In such cases, the daily fluid requirement in the untreated patient may rise to 10 to 12 litres per day and return to near-normal levels in the puerperium. Although the reason for this exacerbation is not clear, it may be related to the considerably increased amounts of adrenocortical hormones which are present in the latter months of pregnancy (Mackay *et alii*, 1957). It is a well-known fact that a normally functioning anterior pituitary lobe is usually necessary for diabetes insipidus to appear. Foukas *et alii* (1954) have postulated that the secretion of the antidiuretic hormone may be inhibited by the adrenocortical hyperfunction, while Swingle *et alii* (1953) have induced a state of diabetes insipidus in adrenalectomized dogs by treating them with cortisone. This could then be corrected with large doses of posterior pituitary extract. Increased amounts of other anterior pituitary hormones may also be implicated, particularly thyrotrophin, as Heinbecker *et alii* (1947) have found that the administration of thyroid to dogs with diabetes insipidus produces an increase in the polyuria. In support of this, Winer (1942) has described amelioration in a case of diabetes insipidus in which a thyroidectomy had been complicated by myxoedema. In opposition to the foregoing findings are those of Leaf *et alii* (1942), who found that anterior pituitary hormones were without effect in a

TABLE II.
Urinary and Serum Electrolyte Values, and Dosage of Pitressin Needed During Pregnancy and the Puerperium (Mrs. A.).

Date (1958).	Weeks of Gestation.	Urine Volume. (Millilitres per Day.)	Urine Electrolytes. (Grammes per Day.)			Serum Electrolytes. (Millequivalents per Litre.)				Dose of Pitressin.
			Na ⁺ .	K ⁺ .	Cl ⁻ .	Na ⁺ .	K ⁺ .	Cl ⁻ .	HCO ₃ .	
February 9 ..	19	2230	3.01	2.23	4.64	—	—	—	—	1 ml. intramuscularly per 48 hours.
March 4 ..	22	2730	5.70	9.25	9.54	140	3.8	109	—	1 ml. intramuscularly per 48 hours.
May 11 ..	32	2800	3.43	2.31	6.06	—	—	—	—	0.5 ml. intramuscularly, 0.5 ml. subcutaneously per 24 hours.
June 21 ..	38	3400	3.85	1.90	6.20	—	—	—	—	0.5 ml. intramuscularly, 0.5 ml. subcutaneously per 24 hours.
July 1 ..	40	1350	3.22	1.91	5.56	142	3.8	107	22.8	0.5 ml. intramuscularly, 0.5 ml. subcutaneously per 24 hours.
July 2 ..	During labour, first day of puerperium.	3800	5.24	1.89	1.89	—	—	—	—	0.5 ml. intramuscularly, 0.5 ml. subcutaneously per 24 hours.
July 3 ..	Second day of puerperium.	3150	3.98	2.25	1.79	—	—	—	—	0.5 ml. intramuscularly per 24 hours.
July 11 ..	Tenth day of puerperium.	1100	4.08	2.25	5.63	145	4.6	117	25.9	1.0 ml. intramuscularly every 3 days.

patient with diabetes insipidus, provided that the urinary solute load was kept constant. These workers could find no effect of cortisone itself on the antidiuretic effect of pitressin.

The disease has been noted to occur in successive pregnancies, with almost complete remissions in the intervening periods (Duncan, 1888; Anselmino and Hoffman, 1930). When the condition has been present prior to the pregnancy, however, there may be no change, or occasionally an improvement may occur (Carter, 1940; Dann, 1951).

One of the most interesting features of the association of these two conditions is the behaviour of the second neurohypophyseal hormone, oxytocin. This substance is generally regarded as playing a significant role in parturition and lactation. This idea received confirmation in the experiments of Fisher *et alii* (1935), whereby cats, in which artificial diabetes insipidus had been produced, usually had prolonged labours; spontaneous delivery did not always occur, and death ensued in some of the animals. A similar occurrence has been described in the human parturient with diabetes insipidus (Maranon, 1947; Lake, 1947). However, such a disturbance in the labour mechanism is by no means common. In the present case, the labour was prolonged, but the aetiological factor was probably a hypertonic type of incoordinate uterine action, which is not uncommon in the primigravida. This explanation is supported by the satisfactory response obtained with continuous epidural anaesthesia. In the majority of the reported cases of diabetes insipidus, particularly the inherited type, labour begins spontaneously, and contractions are of normal frequency, duration and intensity. The third stage is usually uncomplicated. With regard to lactation, there is conflicting evidence about the ability of these patients to breast feed their infants. In the majority, successful initiation and maintenance of breast feeding occur. Isbister (1956) and others have described cases in which a normal draught reflex has been present. This phenomenon, which is the same as the "let-down reflex" in animals, is directly due to the release of oxytocin from the posterior pituitary lobe in response to suckling, with stimulation of afferent nerves in the nipple area. Although lactation was initially satisfactory in the present patient, she experienced no sensation allied to the draught reflex, and although this is not an uncommon occurrence, the sequence of events is suggestive of a possible disturbance in oxytocin release.

Most investigators have reported normal values for the blood volume and serum electrolytes in this disease, and

also for the excretion of the electrolytes and total solids in the urine (Chu *et alii*, 1941; Blotner and Kunkel, 1942). Similar findings were encountered in the present case, apart from the fact that pitressin injections were followed by some reduction in total electrolyte excretion in the urine. A point of interest was the rise in potassium excretion following the administration of sodium chloride. This may be directly related to the salt ingestion, or it may have been a result of the patient withholding her pitressin injections on account of uterine cramps which had followed their administration. Blomherst (1956), discussing the influence of antidiuretic hormone on renal electrolyte excretion, found that as this substance was withheld from his patient with diabetes insipidus, sodium was retained and potassium was lost. The finding, in the present case, of high sodium and low chloride excretion after delivery has not been explained.

With reference to the diagnosis of the condition, usually little difficulty is experienced, although it is surprising to note the degree of acceptance of the disability that some individuals acquire, so that they fail to seek medical aid. In congenital cases, the original diagnosis is often that of enuresis. In a small percentage of cases of the inherited type of the disease, the defect may be in the renal tubule rather than in the hypothalamic nuclei. However, in this group males are predominantly affected. Such cases are characterized by a resistance to pitressin, and on investigation, normal amounts of the antidiuretic material will be found in both blood and urine (Piel, 1957). Both of these conditions can be differentiated from diabetes insipidus of psychogenic origin by the Hare test (Hickey and Hare, 1944). Only in the latter condition will the hypertonic saline infusion produce an antidiuretic response.

With the production of long-acting vasopressin preparations, treatment has been greatly simplified. When cruder preparations were used, some authorities recommended the suspension of all pituitary therapy during pregnancy, fearing that premature labour would otherwise ensue. In one of Blotner and Kunkel's (1942) cases, pituitary extract produced a sense of constriction in the uterus, whereas pitressin itself was without any oxytocic effect. This was not the experience of the present patient, who frequently reacted to the pitressin injections with cramping pains in the uterus. In Hendrick's (1954) first case, painless tonic contractions of the gravid uterus followed the administration of 2 to 4 min. of pitressin, and these persisted for as long as half an hour. There is some evidence to suggest that, in the first half of pregnancy,

pitressin may have an effect on the uterus equal to or greater than that of oxytocin (Layton, 1958). Although snuff has been thought to be less likely to produce premature labour (Green and Gibson, 1939), this again is not a general experience. Train's (1951) patient, who was controlled on this therapy, noted strong contractions for about two hours after the medication had been administered.

In cases in which the disease is of an acquired nature, such as those described by Maranon (1947), it would seem that pituitary extracts containing both hormones are necessary for parturition to occur safely. As was stated earlier, in most cases of the hereditary variety of the disease, there is little disturbance in the reproductive processes. This would indicate that oxytocin is either not required or, more likely, that its production and excretion are to some extent independent of that of vasopressin. In Dandy's case (1940), there had been a surgical incision through the pituitary stalk in the course of an exploratory operation. Although severe diabetes insipidus ensued, subsequent menstrual cycles, pregnancy, labour and the puerperium were all normal. This finding is hard to reconcile with the findings of relatively minute amounts of oxytocin in the hypothalamus compared with the posterior pituitary lobe. One can only surmise that this hormone, unlike pitressin, can reach the circulation directly from the hypothalamus, or that its presence in the above-mentioned physiological functions is superfluous. Only by accurate hormone assay can this be established.

The prognosis for the mother in this disease is very good. There is little, if any, shortening of life if the diabetes is of the inherited type. Some amelioration often occurs after the age of 45 years, and spontaneous and permanent remissions may occur before this time. Toxæmia of pregnancy seems to occur less frequently than is usual. The fetal outlook is likewise good, although there may be some increase in the incidence of prematurity. In the reported cases in which perinatal death occurred, there was usually an obstetrical explanation. As the transmission of the disease is seemingly by a dominant gene (Pender, 1952), there is a definite possibility that the offspring may be affected. Although there have been reports of termination of the pregnancy in the presence of diabetes insipidus, there now appears to be little justification for this measure.

Summary.

1. A case of diabetes insipidus complicated by pregnancy is described.
2. The association of these two conditions seems to occur with a frequency roughly in proportion to the population at large.
3. As is usual in such cases, there was in the case described some aggravation of the diabetes insipidus, with improvement after delivery.
4. The effect of this disease on reproductive function is discussed, and mention is made of the disturbance in oxytocin function which may coexist.

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DIPHYLLOBOTHRIASIS IN FINLAND, WITH SPECIAL REFERENCE TO INCIDENCE, TRANSMISSION AND CLINICAL FEATURES.¹

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DIPHYLLOBOTHRIASIS is a disease of fish-eating mammals infested with the broad tapeworm *Diphyllbothrium latum* (synonym *Dibothriocephalus latus*). The worm leads a parasitic existence in the intestine of the host. The disease occurs in man in communities where the consumption of uncooked or undercooked fresh-water fish is a dietary habit.

Interviews with Intending Migrants.

A random selection of adults from various parts of Finland who presented for the migration interview were questioned about the occurrence of diphyllbothriasis. All were familiar with the disease, and of the 68 questioned 10 gave histories of having had it. The

¹This article has been written specifically for the Australian practitioner whose interest in diphyllbothriasis may have been aroused by contact with Finnish immigrants; hence references made to original articles, particularly the zoological articles, may not indicate the actual scope and true direction of the investigations performed.

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presenting complaints were: varied constitutional symptoms together with proglottid discharge, 2 persons; proglottid discharge only, 3 persons; constitutional symptoms without proglottid discharge, 2 persons. The other 3 persons had no complaints; diagnosis was made by routine stool examination during military service.

The commonest types of fish which are eaten in the uncooked state and which occur in Finland's fresh-water lake system belong to the coregonid species, and are known in Finnish as *Stika* (*Coregonus lavaretus*) and *Mutikka* (*C. albula*). Both are considered delicacies, and they are eaten as early as twelve hours after being salted. This dietary habit is acquired at a very early age; one woman from the Lakes District stated that all her children commenced at about the age of six months.

Incidence.

The State Medical Board of Finland has carried out a comprehensive statistical survey on the incidence of diphyllobothriasis in Finland, and concluded a report in February, 1959 (Laine *et al.*, 1959), which showed that the infestation rate was about 20% of the entire population. This rate was assessed from statistical data based on anthelmintic sales, new cases of infestation notified to the Medical Board, the material compiled from studies of E. V. Venho and I. Venho, and Huhtala's statistics compiled from inquiries. The infestation rate is highest in the Lakes District and in other areas where fish-eating habits are prevalent. In some communes the infestation rate was 15% in children who had just reached school age, and rose with age to about 70%. Only 3.3% of the total population were receiving active anthelmintic treatment. Tables I and II are adapted from the above-mentioned report.

TABLE I.

Incidence of Tapeworm on the Basis of Personal Questionnaires to Physicians.

Authority.	Year.	Comment.
Sievers	1905	Very common in most of the country.
Ehrström .. .	1926	An average of 20% to 25% of the total population, eastern Finland 50%.
Huhtala .. .	1950	An average of 20-15%, eastern Finland 61% to 100%.

Some Characteristics of the Worm Related to Symptomatology.

The adult worm, which can grow to a length of 12 metres, contains no alimentary tract, and absorbs nourishment from the surrounding liquid medium through its cuticular covering. Therefore for survival it must dwell in the small intestine.

It has the ability to change its position in the intestine and can actually progress against the peristaltic flow. The holdfast possesses no hooklets, so that no blood loss occurs at the site of attachment. The bothria of the holdfast have a rather weak gripping action, the worm's position being maintained by circumferential pressure against the intestinal wall. When it is placed high in the small intestine, vomiting of pieces of the worm may occur. Also, this ability to change position is responsible for the appearance or disappearance of one of the major clinical effects of this disease, which will be described later.

The worm is hermaphroditic and contains 2000 to 4000 proglottids. A whole chain of terminal proglottids is actively egg-producing—as many as one million eggs may be produced in one day. The chain usually breaks off in pieces and then undergoes varying degrees of autolysis in its passage down the alimentary canal. Sometimes no proglottid is recognizable in the stool.

Egg production commences within weeks of ingestion of the plerocercoid larva. Wardle and Green (1941 a and b) in experiments on the rate of growth of this worm, infested dogs with plerocercoid larvae, and found that

the first discharge of eggs occurred 18 to 20 days after ingestion of the larvae. Multiple infestation was common.

In man infestation is usually single, but multiple infestation is common in areas where there is a high incidence of the disease. A leading Helsinki physician quoted a case in which a length of 140 metres of worm was expelled from the one individual; there were about 20 worms. Out of 25 infested persons studied by Nyberg (1957), 11 had a single infestation and 14 multiple infestation (ranging from 2 to 20 worms).

The life of the adult worm within the host may last for many years.

Transmission.

There are two larval forms in this worm's life cycle. The first, the procercoid larva, develops from the egg in a fresh-water copepod crustacean, and the second, the plerocercoid larva or sparganum, develops from the procercoid larva in specific fresh-water fish. Man contracts the disease by ingesting viable spargana usually contained in the flesh of diseased fish. Adequate cooking or salting will kill the sparganum.

Errors have occurred in the past in identifying this worm's plerocercoid larval form from other Diphyllobothrid species which also infest fresh-water fish, with

TABLE II.

Incidence of Tapeworm According to Studies of Certain Sections of the Population.

Author.	Year.	Source of Figures.	Total.	Percentage.
Seppä .. .	1927	Patients of a military hospital.	3937	11.3
Mustakallio ..	1940	Résumé of different statistics.	15,192	23.7
Ollilainen .. .	1943	A Northern Finnish regiment.	2768	31.1
Tötterman .. .	1944	Military hospital.	850	17.8
		Civilian patients.	233	66.0
		Civilian out-patient department.	—	41.4
		The following year.	2006	14.5
Setälä .. .	1945	Kärkölä.	2097	59.0
Gylling .. .	1949	Military records.	14,631	18.0
Tähti .. .	1952	Hankasalmi elementary school.	1226	15.8
Venho-Venho ..	1953	Conscripts.	957	21.7
Uurasmaa .. .	1958	Inari (15% of population).	988	6.2
		Saarijärvi (5% of population).	592	6.3

the result that some confusion has arisen in determining the true nature of the fish intermediate hosts.

The fish in the Lakes District of Finland which have always been thought to be mainly responsible for the transmission of the disease to man are *Stika*, called whitefish in English and *Mutikka*. Both fish feed on plankton (copepoda form part of zooplankton), and so in these waters, which are polluted with the sewage of innumerable tapeworm hosts, they should be, if susceptible, heavily infested with plerocercoid larvae. Wikgren and Muroma (1956), using Kuhlow's differential diagnosis of diphyllobothrid plerocercoid larvae, have shown that the plerocercoid larvae which are to be found in the coregonids (*Stika* and *Mutikka*) are those of the tapeworm *D. osmeri*, a parasite of gulls. No plerocercoid larva of *D. latum* was found.

Vik (1957) has examined fish from eastern Norway for *D. latum* plerocercoid larvae. His results are listed in Table III.

Feeding experiments in man showed that the plerocercoids found in pike and perch were those of *D. latum*.

The fish so far known which can act as transport hosts for plerocercoid larvae of *D. latum* to man are pike, perch, burbot (*Lota vulgaris*), ruff (*Acerina cernua*) and probably trout (*Salmo trutta*) and char (*S. salvelinus*).

The question arises how these fish, which do not eat plankton, become infested. Wikgren and Muroma (1956) put forward the suggestion that the larger predatory fish, pike and burbot, take over plerocercoids only from smaller predatory fish, ruff and perch, upon which they prey. Small ruff and perch are susceptible to the procercoid larva, and whilst young feed on plankton for a

considerable period of time. The same authors provisionally assumed that *D. latum* did not at all pass through plankton-feeding fish species.

However, Vik (1957), whilst working on the life cycle of another fish tapeworm parasite of man, *D. norvegicum*, occurring in Norway, and on the transmission of the plerocercoid larva of *D. latum*, found that the nine-spined stickleback (*Gasterosteus pungitius*) was susceptible to the proceroid larva of both of these worms. The stickleback spawns in fresh water in summer and afterwards migrates down to the sea. In the fresh-water lakes it forms part of the diet of the pike, and in the Baltic it probably forms the chief food of salmon (*S. salar*). There does not appear to be any definite work as yet indicating that salmon is a transport host of the plerocercoid larva of *D. latum*. Formerly in Finland it was generally assumed that the poorer peoples of the Lakes District acquired the disease by eating *Sika* and *Muikku*, whilst the wealthier city people acquired it by eating lightly-smoked salmon. The disease is far less common in the city.

No truly marine fish has been known to transmit the disease to man.

TABLE III.

Results of Examination of Different Species of Fish (Vik, 1957).

Fish Species.	Number Examined.	Number Infected.
<i>Coregonus lavaretus</i> (whitefish)	173	0
<i>Esox lucius</i> (pike)	20	16
<i>Perca fluviatilis</i> (perch)	31	15
<i>Thymallus vulgaris</i> (grayling)	2	0

Epidemiology.

The disease is transferred from one place to another by man, and the maintenance of the disease depends upon all the conditions necessary for completion of the worm's life cycle.

Bearup (1957) has shown that the autochthonous copepods *Boeckella minuta* and *Gladioferens brevicornis* collected from fresh-water lakes about Sydney were suitable vectors for the first larval stage (in Europe copepoda belong to the genus *Diaptomus* or *Cyclops*). It has also been reported that suitable *Diaptomus* species are to be found in Australia.

There are enough immigrants from Finland and the other Baltic ring countries (all are endemic centres of the disease) to ensure that the dietary habit of consuming uncooked fish continues. In fact, uncooked fish is eaten in most European countries in one form or another (salted, pickled or flavoured with onion); however, it is usually marine fish.

Quite a large number of immigrants with asymptomatic diphyllobothriasis must have entered the country already; therefore a reservoir of worms exists. However, the lack of a large supply of fresh-water fish and the presence of efficient sanitation control in Australia will prevent this disease from becoming a public health problem.

Dogs are also hosts to the disease; but the eggs of *D. latum* when harboured by a dog are reputed to have a very low fertility rate.

The odd case of diphyllobothriasis will be seen in practice; therefore an understanding of the clinical aspects of this disease is important.

Symptomatology, Pathology and Pathogenesis.

Gastro-intestinal symptoms, such as diarrhoea, constipation, anorexia, excessive appetite, nausea and colic, are usually the main complaints. Proglottid discharge is often an accompanying complaint, but not necessarily so. Frequently the host has no complaint whatsoever. Occasionally the patient develops an acute abdominal condition which may be difficult to diagnose. Laparotomy has been performed for a suspected peptic ulcer perforation (Von Bonsdorff, 1947). Also the acute abdominal

symptoms may simulate acute appendicitis, intestinal obstruction or gall-stone colic.

Vomiting of pieces of worm occasionally occurs; the subjective sensation associated with this is that of suffocation. In these cases macrocytic anaemia is often observed. The anaemia resembles true pernicious anaemia. There were two schools of thought concerning the cause of this anaemia, one adhering to the concept that a toxic substance (Wardle and Green, 1941 a and b), the product of worm autolysis, was absorbed from the intestine into the blood-stream and so interfered with haematopoiesis, and the other to the concept that the worm somehow or other interfered with the formation or absorption of the haematopoietic principle (Von Bonsdorff, 1947). The latter proved to be correct. Other features about this anaemia were that it responded to liver therapy, its onset bore no relation to the duration of the disease (that is diphyllobothriasis), and it sometimes underwent spontaneous remission.

In 1947 Von Bonsdorff carried out intubation experiments, listed below, on 26 known tapeworm carriers. First he made estimations of the length of tube required to reach the various parts of the alimentary tract from the mouth. Radiological aids were used in these determinations. He found the following to be average lengths in adults: distance from mouth to pylorus, 56 to 60 cm.; distance from mouth to duodeno-jejunal flexure, 70 to 80 cm.; distance from mouth to jejuno-ileal boundary, 140 to 150 cm.; distance from mouth to ileo-colic valve, 250 to 300 cm.; distance from mouth to anus, 250 to 300 cm.

There was some difficulty in passing the tube through the ileo-colic valve, so either the bowel stretched or the tube unwound. In the living state the length of the adult alimentary canal measured by intubation is between 2.5 and 3 metres. In the cadaver the intestine has lost its muscle tone and is much longer.

In the 26 tapeworm carriers, measurements of length were made when eggs were aspirated. Often on withdrawal of the tube, healthy-looking proglottids were found adhering to its end. The clinical findings are set out in Table IV. This showed that worms at a high alimentary site were associated with the anaemia.

TABLE IV.

Relationship of Anaemia to Position of Tapeworm (Von Bonsdorff, 1947).

Condition of Blood.	Number of Cases.	Distances at which Eggs and/or Proglottids were Found on Intubation.	Site.
Normal blood picture	10	130 to 235 cm.	Ileum.
Non-pernicious anaemia (other causes)	3	140 to 334 cm.	Ileum.
Pernicious anaemia manifest	10	95 to 135 cm.	Jejunum.
Pernicious anaemia in spontaneous remission	3	205 to 320 cm.	Ileum.

In later work (Von Bonsdorff, 1956) it was shown that the tapeworm pernicious anaemia was always haematologically and clinically identical with genuine pernicious anaemia, neurological manifestations included. The neurological manifestations are those due to subacute combined degeneration of the cord and peripheral neuronal degeneration. The administration of folic acid improves the blood picture but worsens the nerve lesions.

In Finland no hypochromic anaemia has ever been attributed to *D. latum*. If a patient did suffer from both diphyllobothriasis and hypochromic anaemia at the same time, the anaemia was not relieved without further treatment after expulsion of the worm.

In tapeworm anaemia the erythrocyte count may fall to a range from 500,000 to 1,000,000 per cubic millimetre and the haemoglobin value to less than 20%. The colour index is more or less increased, but often the rise is

less marked owing to the presence of various erythrocyte populations. The mean diameter of the red cell is increased, as is its volume. Polikilocytosis and anisocytosis are present with a preponderance of macrocytes. Occasionally nucleated erythrocytes, normoblasts and megaloblasts are encountered. The thrombocyte count may be reduced to values below 20,000 per cubic millimetre, with the result that the bleeding time is prolonged and a tendency to haemorrhage is present.

With a blood picture like that described above, the main presenting symptoms of a person suffering from diphyllorhynchiasis will be those of the anaemia.

The gastric juice in *D. latum* anaemia contains Castle's intrinsic factor, but commonly the gastric secretions are reduced. This effect appears to be secondary to the anaemia.

The cause of the pernicious anaemia of diphyllorhynchiasis is vitamin B₁₂ deficiency in the host as a result of uptake of this vitamin by the worm. The worm appears to need this substance in its growth processes, and contains a high concentration of it in its substance. Von Bonsdorff in experiments (1956) showed that the extract of dried expelled worms contained large quantities of extrinsic factor. He also presented the following observations:

1. In patients with pernicious anaemia due to *D. latum*, and also in patients with true pernicious anaemia, remissions followed intramuscular injections of an aqueous solution of extracts of dried tapeworm. The same results were obtained with injections of vitamin B₁₂. There were no untoward effects—that is, the tapeworm extract was not toxic—and there was a remission of both the haematological and neurological symptoms.

2. Genuine pernicious anaemia was successfully treated by the oral administration of any one of the following three combinations: (i) stomach extract (contains intrinsic factor) and meat (contains extrinsic factor); (ii) stomach extract and extract of dried tapeworm; (iii) stomach extract and vitamin B₁₂.

3. Pernicious anaemia of *D. latum* might or might not respond to such treatment; more often than not it did respond. Similar results were obtained when meat, extract of dried tapeworm or vitamin B₁₂ was given alone. That is, in pernicious anaemia of *D. latum*, no extra supply of intrinsic factor was necessary.

Nyberg (1958 a and b), in experiments on the uptake of vitamin B₁₂ by the host and parasite, used vitamin B₁₂ labelled with radio-active cobalt (Co⁶⁰). He measured the amounts taken up by the worm, the level in the host's blood-stream and the urinary excretion. When small, "physiological" doses were administered, it was found that worms placed in the proximal part of the small intestine absorbed an average of 89.5%, whilst those more distally placed absorbed an average of 44.3% of the administered dose. Additionally, in two cases of genuine pernicious anaemia, the worm's ability to absorb vitamin B₁₂ was not affected; this showed that the worm was not dependent on intrinsic factor. Nyberg also found that there was a definite pattern to the uptake of vitamin B₁₂ in the worm. The concentration of vitamin B₁₂ in the worm was maximal at the zone of greatest growth—that is, that section distal to the neck. Therefore the process of absorption of vitamin B₁₂ must be an active one, and not just one of simple diffusion. This need of *D. latum* for vitamin B₁₂ is quite remarkable, as the concentration in *Taenia saginata* is 50 times less. Co⁶⁰ given alone was found not to be absorbed.

Nyberg, Gräsbeck and Sippola (1958), using Schilling's urinary radio-activity test, showed that in both anaemic and non-anaemic tapeworm carriers there was a significant decrease in the excretion of radio-active vitamin B₁₂ when compared with the healthy subject. This is due to low blood levels of vitamin B₁₂.

In a recent investigation in the Lakes District in Finland, Nyberg found that almost all carriers of *D. latum* had a serum vitamin B₁₂ level below the normal value, whether anaemia was manifest or not. About 1 in 50 showed megaloblastic anaemia, but none had any

complaints. In these cases anaemia would probably become manifest if the diet was poor (as happened in Finland in 1942—a large number of cases of anaemia) or if the carrier suffered from some febrile disease.

Therefore, for the production of anaemia, the tapeworm must be proximally placed. The anaemia may appear many years after the host has ingested the sparganum, by virtue of the worm's ability to change position from a more distal to a more proximal region of the small intestine and thus interfere more efficiently with the host's absorption of vitamin B₁₂. Or conversely, spontaneous remission of anaemia may occur when the worm moves distally or is discharged. The size of the worm has little effect on the pathogenesis of the anaemia.

Spontaneous discharge of the worm is frequent.

Distinguishing Features Between Pernicious Anaemia of *D. latum* and Genuine Pernicious Anaemia.

The two types of pernicious anaemia may be distinguished as follows: (i) The onset of pernicious anaemia of *D. latum* is earlier—it can occur under the age of 20 years. (ii) After discharge of *D. latum*, sternal puncture shows a change in the cells from megaloblastic to normoblastic within two days, without any specific therapy for the anaemia. (iii) Once the worm has been discharged, no further haematological therapy is necessary—there is a complete remission. In genuine pernicious anaemia, therapy is required for the remainder of the patient's life. (iv) Pernicious anaemia of *D. latum* usually responds to the oral administration of vitamin B₁₂ given alone. (v) In pernicious anaemia of *D. latum*, there is usually free hydrochloric acid present in the stomach.

Diagnosis.

Diagnosis depends on the finding of eggs of *D. latum* in the stool. Several tests at daily intervals should be performed.

Treatment.

Treatment lies in the expulsion of the worm, and if anaemia is present, it should be dealt with before the vermifuge therapy is commenced.

Sodeman and Jung (1952) confirmed the findings of Latin American workers in the use of "Atebrin" (quinacrine hydrochloride) as an effective vermifuge in intestinal cestodiasis. Their régime was as follows:

1. On the day preceding specific drug therapy: (i) Liquid diet. (ii) Mid-afternoon purge with either magnesium sulphate or sodium sulphate. The effect of this purgation should be noted so that the dosage for the post-vermifuge purge can be modified. The object of this is to eliminate roughage, so as to expose the worm to the action of the anthelmintic drug.

2. On the day of specific drug therapy: (i) Early morning: administer 0.1 gramme tablets of quinacrine hydrochloride two at a time with water every five minutes, up to a total of eight. If nausea is produced, add sodium bicarbonate to the water. If vomiting occurs, the number of tablets can be counted in the vomitus, and the lost number given again with water containing sodium bicarbonate. (ii) Two hours later: administer the purgative. Food is withheld until there is a bowel action.

The dosage described is for an adult. More recently it has been found that a single dose of 0.5 gramme given together with sodium bicarbonate is effective. For children the dose should be reduced according to size.

In Finland, aspidium (filix mas) is still used. It is found to be very effective in expelling *D. latum*, but not so effective with the *Taenia*.

Usually the worm is expelled in an intact or fragmented state, and with "Atebrin" therapy it is stained yellow. It may be sluggishly motile. However, cases have been reported in which no worm was expelled, but the patients were declared cured as a result of the failure to find any eggs of *D. latum* in repeated stool tests. If no worm is expelled, or if the head is not to be found in the mass of expelled worm, then follow-up stool tests should be performed.

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AN EVALUATION OF THE AZURE A CARBACRYLIC RESIN DIAGNOSTIC TEST ("DIAGNEX BLUE") FOR GASTRIC ACIDITY.

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It has been thought for many years that the estimation of gastric acidity by means of intubation was somewhat unsatisfactory and rather distressing to most patients. Furthermore, it would appear that the results were to some extent influenced by the attendant physical and psychological stress.

After the introduction of ion exchange resins, a method was evolved by Segal, Miller and Morton (1950), using a quinine resin compound. Unfortunately, estimation of the amount of quinine liberated was possible only by the use of a fluorometer, and this rendered it impracticable in most cases. However, in 1955 Segal, Miller, and Plumb simplified this tubeless technique by the use of a carbacrylic resin linked with Azure A as the indicator dye. In the presence of free hydrochloric acid, this dye is released from the resin complex and excreted in the urine, although it has been noted that insignificant amounts of the dye may be released from the complex by electrolytic ions. When the resin compound is taken orally, the free hydrochloric acid releases the dye, which is absorbed by the small intestine, passed into the blood-stream and excreted by the kidneys.

It will be appreciated that certain conditions will necessarily interfere with the chain of events leading to a proper execution of the test. Vomiting and/or pyloric obstruction will prevent the absorption of dye in the small intestine, and the normal urinary excretion may be affected by severe malabsorption, cardiac failure and dysfunction of the liver and kidneys.

Method.

The procedure is as follows.

Collection of Specimens.

The patient fasts from midnight on the day of the test, urinates on rising and discards the specimen. Two tablets, each containing 250 mg. of caffeine sodium benzoate (gastric stimulant), are taken with a glass of water. One hour later the patient empties the bladder, and the whole specimen is retained as a control. Then 2 grammes of resin-dye-compound, in the form of granules (containing 100 mg. of Azure A dye), are swallowed with water. Two hours later the patient empties the bladder, and this comprises the test sample.

Determination of Azure A Dye in the Urine.

Procedure A.—Both control and test specimens of urine are diluted with water to a volume of 300 ml. each, and the colour of the test urine is compared in a simple comparator block supplied, which comprises two standards equivalent to 0.3 and 0.6 mg. of dye excreted.

Procedure B.—If the test sample colour is less than the 0.6 mg. standard, it is recommended that samples be acidified with 6N hydrochloric acid (one drop), heated in a boiling water bath for 10 minutes and allowed to cool before the colour intensity is estimated.

TABLE I.

Dye Excreted.	Findings.	Percentage of Subjects.
0 to 0.3 mg.	Achlorhydria.	21
0.31 to 0.6 mg.	Borderline achlorhydria.	9
0.61 to 0.99 mg.	Hypocidity.	10
1.0 to 2.0 mg.	Normal acidity.	37
Over 2.0 mg.	Hyperacidity.	23

Results.

Readings of 0.3 mg. or less indicate achlorhydria, and readings between 0.3 and 0.6 mg. are regarded as indicating borderline achlorhydria. However, we have found that this process of acidification is an essential part of the technique of the test, since it would appear that full development of the dye excreted can be demonstrated only on boiling at a low pH.

Although certain authors, including Gilbert (1957), and Raskin *et alii* (1959), have indicated that this technique yields qualitative results only, we have thought that an improved method of estimation of dye excretion could be adapted to give results of quantitative nature.

The amount of dye released must be directly dependent upon the concentration of acid in the stomach, and dye set free is thereupon absorbed from the small intestine. Since tests are carried out under standard conditions, urine samples are collected at a set period of two hours and such samples are diluted to a constant volume, then the final concentration of colour must, we hold, be a fair index of the hydrochloric acid concentration present in the stomach. Thus, all colour estimations have been carried out with an E.E.L. photoelectric absorptiometer with a light filter 607 (wave-length 600 Å), and standards were prepared from suitable dilutions of dye.

Initial trials of a batch of normal controls (laboratory staff, nurses, etc.) showed the normal excretion to be between 1.0 and 2.0 mg. of dye.

One hundred patients requiring gastric investigation have been examined by this method, and the results obtained are shown in Table I. A wide range of results was found, varying from zero to 4.7 mg.

To confirm the foregoing findings, these patients were subjected to intubation, and comparable results were obtained. However, 26% of the patients with achlorhydria responded to the administration of histamine and showed their condition was not histamine-fast.

Discussion.

This appears to be a most useful, reliable and easy test, causing no distress to the patient.

We believe that this cannot be regarded as a "bedside" method, in view of the necessity for the acidification and boiling of specimens in all cases. However, when readings can be carried out on a suitable photoelectric absorptometer, this method is ideal for use in hospital and other laboratories, and results can be successfully tabulated as achlorhydria, hypoacidity, normal acidity or hyperacidity.

It is interesting that we have found a high degree of achlorhydria here, and this has been confirmed by intubation also. These cases are of functional nature, and not due to pernicious anaemia or gastric carcinoma. Many patients complaining of symptoms which might appear to be due to hyperacidity are in fact achlorhydric and naturally respond to replacement therapy, while antacids have a deleterious effect.

Summary.

1. One hundred cases have been investigated by means of the Azure A carbacrylic resin diagnostic test ("Diagnex Blue").

2. The method has been adapted to give quantitative results, and readings have been carried out with the E.E.L. photoelectric absorptometer.

3. It has been found possible to interpret results under the headings of achlorhydria, hypoacidity, normal acidity and hyperacidity.

4. The foregoing results have been confirmed by the intubation method.

Acknowledgement.

Our thanks are due to E. R. Squibb & Sons, Ltd., for the supply of "Diagnex Blue".

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Reports of Cases.

UNUSUAL REACTIONS TO ANTI-TUBERCULOUS CHEMOTHERAPY.

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We have recently investigated two cases of unusual reactions to anti-tuberculous chemotherapy—the first a case of jaundice after INAH administration, possibly precipitated by hypersensitivity to PAS, the second a case of renal symptoms with hyperuricaemia due to pyrazinamide, but without joint involvement.

Case 1.

Hepatitis due to isonicotinic acid hydrazide has only rarely been described (Randolph and Joseph, 1953; Gellis and Murphy, 1955). The drug is widely used in the treatment of tuberculosis, and toxic effects of any kind are uncommon even with very high dosage. Harris (1959) reported only two cases of peripheral neuritis and one of psychosis in a series of 127 patients who had received as much as 1200 mg. of INAH per day.

The patient was a housewife, aged 36 years, who had had infective hepatitis in childhood. She had been diagnosed as having pulmonary tuberculosis in 1945 and treated satisfactorily at that time by bed rest in hospital and a right artificial pneumothorax. This was abandoned after some years, and she remained well until May, 1959, when she developed influenzal symptoms with fever, cough, dark brown sputum and pain in the left side of the chest. She was treated by her own doctor with penicillin given systemically. After two weeks, an X-ray examination of her chest revealed cavitation in both middle zones, and she was admitted to another hospital on June 2. Examination of her sputum revealed tubercle bacilli, and treatment was begun with streptomycin (2 grammes on alternate days), PAS (12 grammes) and a high dosage of INAH (900 mg. per day); the penicillin was also continued for a further two weeks. Six days after her admission to hospital, she developed an erythematous rash and vomiting, and PAS was discontinued. Four days later she developed jaundice. Her liver was enlarged, her stools became pale and bile was present in the urine. The elevated temperature, which had been subsiding, rose again to nearly 101° F. for two evenings. The dosage of INAH was reduced to 300 mg. per day and discontinued after three days. The jaundice rapidly subsided and the liver size decreased to normal. PAS therapy was resumed as calcium benzoyl PAS with no ill effects at first, the streptomycin having been continued throughout, and the patient was admitted to the Morris Hospital a fortnight later on July 2.

On her admission, she was well and had no symptoms, and her liver was not enlarged. On July 14 she developed a generalized macular erythematous rash, which subsided after PAS was discontinued and reappeared after a test dose was given three days later. Accordingly, PAS was not resumed, and it was intended to give streptomycin with another drug; but, after two days, a further rash developed around the site of a streptomycin injection and she had some vertigo, so this drug was then also discontinued.

Since the cessation of chemotherapy her general condition has remained satisfactory, and the latest postero-anterior and lateral films and lateral tomography show only a small thin-walled cavity lying in the region of the lingula, the appearances on the right side having returned to those on films taken before her latest illness. With this comparatively rapid X-ray clearing, despite the difficulties with anti-tuberculous chemotherapy, the possibility must arise of there having been a superimposed staphylococcal infection. Initial sputum examinations showed coagulase positive staphylococci in addition to acid-fast bacilli, whose presence was confirmed by culture.

A liver biopsy was performed on August 18, nine weeks after the subsidence of jaundice, and examination of sections showed liver tissue in which the parenchymal cells exhibited a moderate degree of fatty change; there was an increase in the number of cells in the portal tracts, and some eosinophils were present. The normal lobular architecture was well preserved. Liver function tests have been carried out weekly since her admission to the Morris Hospital, and results are shown in Table I, together with serial leucocyte counts.

Discussion.

The features of the results of the liver function tests are the increased zinc sulphate turbidity and cephalin cholesterol flocculation over a prolonged period with normal serum alkaline phosphatase and transaminase

levels. A section of the liver biopsy has the appearance of subsiding cholangiolitic hepatitis, such as is seen in the latter stages of hepatic reaction to chlorpromazine and methyl testosterone, and therefore a sensitization type of response (Professor C. R. B. Blackburn, personal communication).

Cholangiolitic hepatitis may also occur as a hypersensitivity reaction to PAS (Hensler *et alii*, 1957). However, although the present patient developed a rash due to PAS six days after commencement of PAS therapy,

week before the commencement of INAH therapy. Cross-sensitization between INAH, salicylates and PAS may occur. Friedman (1955) described a case in which recrudescence of a severe hypersensitivity reaction, initially due to PAS, occurred after the administration of acetylsalicylic acid, and again as soon as INAH therapy was resumed. On all three occasions liver enlargement was part of the clinical picture.

In the present case, the abnormal flocculation with a normal serum alkaline phosphatase level at first suggested

TABLE IA.
Case I: Results of Liver Function Tests.

Test or Estimation.	June 16	July 14	July 21	July 28	August 4	August 11	August 18	August 25	September 1	September 8
Total serum bilirubin content (milligrammes per 100 ml.)	5.0	0.85	—	—	0.35	0.15	0.7	0.5	0.35	0.35
Colloidal gold turbidity (units)	5	2	—	—	3	0	0	0	1	—
Cephalin cholesterol-flocculation	++++	+++	—	+++	+++	++	+	++	++	Negative.
Zinc sulphate turbidity (units)	26.6	14.7	—	14.7	17.3	14.7	11.3	11.3	16.0	11.3
Total serum protein content (grammes per 100 ml.)	5.8	6.2	—	6.0	6.8	6.5	7.1	6.1	7.2	7.0
Serum alkaline phosphatase content (King-Armstrong units per 100 ml.)	8	8.2	—	5.0	4.5	4.5	5.5	5.5	6.0	5.0
Serum glutamic oxaloacetic transaminase (Sigma-Frankel units)	—	—	12	—	—	—	—	—	—	—
Serum glutamic pyruvic transaminase (Sigma-Frankel units)	—	—	5	—	10	12	10	18	—	—
Quinine oxidase (units) (Roman and Dulmonis, 1959)	—	—	5	—	1	3	2	4	—	—
Prothrombin activity	—	—	—	—	—	77%	—	—	—	—

TABLE IB.
Case I: Haemoglobin Value and Blood Cell Counts.

Estimation.	June 3.	June 12.	June 16.	July 20.	August 4.	August 13.
Haemoglobin value (grammes per 100 ml.)	13.1	12.6	12.3	13.1	14.5	14.0
Erythrocytes (millions per cubic millimetre)	4.3	—	—	—	—	—
Leucocytes per cubic millimetre	15,200	16,500	9300	8000	8000	5100
Polymorphs	—	—	—	41%	61%	39%
Lymphocytes	—	—	—	54%	36%	59%
Eosinophils	—	—	—	2%	2%	1%

she was not receiving PAS at the time of development of jaundice, was subsequently able to take PAS for nearly one month before developing another untoward reaction, and had no recurrence of jaundice or deterioration in liver function and no eosinophilia in the blood during that period.

On the other hand, in the case of INAH jaundice reported by Randolph and Joseph (1953), liver biopsy at the time of the jaundice revealed acute hepatitis (superimposed on a relatively mild degree of cirrhosis of the liver), unlike the lesions seen in chlorpromazine jaundice;

toxic hepatitis; but the subsequent history, the normal transaminase levels (Annotation, 1958), and the liver biopsy result make it certain that this was a sensitization type of response of the liver to INAH, and it is possible that this was precipitated by the preceding mild hypersensitivity reaction to PAS.

Case II.

With pyrazinamide, although it has considerable anti-tuberculous activity, the therapeutic value is handicapped by serious hepatotoxic effects. Morrissey *et alii* (1958)

TABLE II.
Case II.

	August 21.	August 28.	September 8.	September 9.	September 10.	September 11.
Daily dosage of pyrazinamide	3 grammes	—	1 gramme	1 gramme	2 grammes	2 grammes
Daily dosage of "Probenecid"	—	2 grammes	2 grammes	2 grammes	2 grammes	2 grammes
Blood uric acid level (milligrammes per 100 ml.)	7.6	3.0	—	3.4	3.0	2.0
Urinary urate excretion (24 hours)	—	0.6 gramme	0.8 gramme	—	—	—
Blood urea nitrogen content (milligrammes per 100 ml.)	10	—	—	—	—	—

the description resembled that given to the liver in cases of jaundice due to "Marsilid" (isopropyl-INAH). However, in both cases of INAH jaundice reported in detail in the literature, there had been a preceding episode of hypersensitivity to another drug, in one to PAS two years previously, in the other to streptomycin just under a

reviewed the literature and found an incidence of jaundice of 4.4% in 801 patients treated with pyrazinamide. Therefore, its use tends to be limited to patients who have ceased to respond to the three major anti-tuberculous drugs. Pyrazinamide therapy may also result in an elevation of the blood uric acid level. Among

patients receiving pyrazinamide and INAH, Cullen *et alii* (1956) reported three cases of gout, although there was no clinical evidence of renal calculi or tophi.

The patient was a man, aged 47 years. He had first been diagnosed as suffering from pulmonary tuberculosis in 1954, and had had a number of periods of hospital treatment before his admission to the Morris Hospital on June 12, 1959. A postero-anterior X-ray film of the chest and tomography after his admission demonstrated cavitation in the upper lobe of the right lung. Sputum culture produced a positive result, and the organisms were resistant to streptomycin, PAS and INAH. Treatment with pyrazinamide (3 grammes per day) and cycloserine (250 mg. per day, gradually increased to 750 mg. per day) was begun on August 2, as a preparation for possible resection of the upper lobe of the right lung. There were no toxic effects, until on August 20, he experienced a sudden severe attack of right renal colic with slight hæmaturia, 17 days after the commencement of chemotherapy. He had never had any previous similar attacks, there was no history of renal disease, and routine urine examinations had shown no abnormality. A postero-anterior X-ray film of the abdomen revealed no radio-opaque renal stones, and subsequent intravenous pyelography one week later produced a completely normal result. Sixteen hours after the last dose of pyrazinamide, the blood urea nitrogen level was 10 mg. per 100 ml., but the blood uric acid level was raised to 7.6 mg. per 100 ml. The blood uric acid level fell to 3 mg. per 100 ml. after one week, and was not subsequently raised after pyrazinamide therapy was recommenced together with probenecid, a renal tubular blocking agent, although on September 10 he developed slight renal colic of brief duration on the opposite side.

Table II shows the results of the relevant laboratory investigations in relation to pyrazinamide and probenecid administration, and Table III gives the results of serial liver function tests.

TABLE III.

Results of Liver Function Tests, Case II.

Test or Estimation.	July 28.	August 11.	August 18.	August 25.
Total bilirubin content (milligrammes per 100 ml.)	6.5	0.7	0.15	0.7
Colloidal gold turbidity (units)	2	1	2	1
Cephalin cholesterol flocculation	+++	Negative.	+	++
Zinc sulphate turbidity (units)	12	10.7	10.7	12
Total serum protein content (grammes per 100 ml.)	6.3	6.5	7.2	4.8
Serum alkaline phosphatase content (King-Armstrong units per 100 ml.)	4.5	8.5	7	4.0
Serum glutamic pyruvic transaminase (Sigma-Frankel units)	8	8	8	18
Quinine oxidase (units)	5	0	3	2

Discussion.

As the results of liver function tests, particularly transaminase levels, were normal before the commencement of therapy except for the cephalin-cholesterol reaction, this was thought to be no contraindication to treatment, and in fact, this response itself became weaker during the course of treatment.

Hyperuricæmia with pyrazinamide therapy probably has a renal cause (Cullen *et alii*, 1956), and the renal tubular reabsorption of uric acid is increased (Mandel *et alii*, 1958). This effect is independent of the hepatotoxicity of the drug, and is presumably selective for uric acid, as there is no alteration of tubular reabsorption of phosphorus, although phosphorus and uric acid are apparently reabsorbed by the renal tubules in a similar fashion (Mandel *et alii*, 1958). In the present case, there were no joint pains or episodes of arthritis. The sole manifestation of the hyperuricæmia was the unusual one of renal colic, presumably due to precipitation and passage of

urate crystals resulting from the disturbance to normal uric acid excretion.

Summary.

Two unusual reactions to antituberculosis drugs are described, one of cholangiolitic hepatitis due to INAH, the other of hyperuricæmia due to pyrazinamide manifested solely by renal symptoms.

Acknowledgements.

Our thanks are due to Professor C. R. B. Blackburn for his opinion on the liver biopsy section and his helpful advice, and to Dr. W. Roman for the biochemical estimations.

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Reviews.

A Synopsis of Anaesthesia. By J. Alfred Lee, M.R.C.S., L.R.C.P., M.M.S.A., F.F.A.R.C.S., D.A.; Fourth Edition: 1959. Bristol: John Wright & Sons, Limited. 7 1/2" x 4 1/2". pp. 616, with 69 illustrations. Price: 27s. 6d. (English).

ANÆSTHETISTS are fortunate in having this accurate and complete synopsis of their speciality. J. Alfred Lee's fourth edition maintains the high standard of its predecessors, and every practising anaesthetist will benefit by keeping a copy for ready reference. For examinees (and, apparently, some examiners) it is essential reading.

The continued rapid growth of anaesthesia has been covered by inclusion of new chapters and complete revision of the entire text. The place of the phenothiazine derivatives in anaesthesia has merited a complete section, and a good review of induced hypothermia has been added. Halothane has been included in the section on inhalation anaesthesia, and there is a table listing the properties of all the inhalational agents. In keeping with modern practice, the space given to the uses of myo-neural blocking agents is considerably increased, and the antagonists to the blocking agents are fully discussed.

The section in which the choice of anaesthetic is discussed relative to the type of operation is improved by revision of the activities of the adrenal glands. Emphasis is placed on primary and secondary causes of adrenal failure, and the management of blood pressure during surgery for pheochromocytoma is described. The choice of anaesthetics for children now includes a discussion of the uses of relaxant drugs and, most importantly, a chart of tidal volumes related to age.

Chronic pulmonary emphysema, which is a common problem in older surgical patients, is thoroughly discussed. Myasthenia gravis is uncommon, but of special importance to anaesthetists because of its similarity to curariform block, and is included in the same section. The chapter on shock has been completely rewritten, with the emphasis on the loss

of circulating fluid volume, which is being increasingly recognized as its only treatable cause.

The hazard of vomiting during obstetrical anaesthesia has caused increasing concern among anaesthetists in recent years, and the importance of precautions for avoiding this catastrophe is reflected in a completely revised section on anaesthesia and analgesia in labour.

Intermittent positive pressure inflation of the lungs is now shared by therapeutics and anaesthesia, and this edition deals fully with respiratory insufficiency due to lung disease, anterior poliomyelitis and tetanus.

With the remarkable variety of new drugs synthesized each year, there is more emphasis on the relationship between chemical structure and pharmacology. Structural formulae are now included for most of the drugs used. It is regrettable that all doses are not metric, in conformity with the British Pharmacopoeia, especially as B.P. names are used exclusively.

The volume is well printed and strongly bound. Although the price has risen, the book is inexpensive by present standards. Its continued wide popularity is certain.

Experimental Surgery: Including Surgical Physiology. By J. Markowitz, M.B.E., M.B. (Tor.), Ph.D., M.S. in Exp. Surg. (Minn.), J. Archibald, D.V.M., M.V.Sc., Dr. Med. Vet. (Glessen), M.R.C.V.S., and H. G. Downie, D.V.M., M.S. (Cornell), M.V.Sc.; fourth edition; 1959. Baltimore: The Williams & Wilkins Company. Sydney: Angus & Robertson, Limited. 9" x 5", pp. 944, with 580 illustrations. Price: £6 17s. 6d.

THE authors have compressed into the 900 pages of this book, a large amount of information collected from the textbooks and journals of physiology, surgery and veterinary medicine. From these pages, the reader can learn how to produce Perthes' disease in the femur of the rabbit, and how to treat it in the dog by excision and femoral-head prosthesis; he can learn to decerebrate a dog, castrate a cat and transplant a heart, or produce defects in it simulating congenital anomalies. But, for readers who may think that a transplanted organ is a mine of scientific information, they give as a sub-heading to the chapter, Mark Twain's definition of a gold-mine: "A hole in the ground surrounded by liars."

The research worker who wishes to verify an hypothesis by experimental surgery in the animal laboratory would probably devise for himself the operations best suited to his purposes. But, nevertheless, this textbook may be helpful, because of its descriptions of methods already devised, and because of the numerous references to the literature which it provides.

For the teacher of surgery using animal surgery as a method of developing the technique and dexterity of future surgeons, and for the teacher of physiology preparing experimental demonstrations, the book should prove very useful.

The early chapters, on the anti-vivisection movement in the United States of America, and on care and feeding of animals, are of general interest.

The Child with a Handicap: A Team Approach to his Care and Guidance. Edited by Edgar E. Martner, M.D.; 1959. Oxford: Blackwell Scientific Publications. 9" x 6", pp. 435, with illustrations. Price: 82s. 6d. (English).

IN the introduction to this book the editor comments on the complete transformation that has taken place in the last decade in the care and treatment of children with handicaps. This book exemplifies this truth. Twenty-seven specialists in various aspects of child care have combined their talents to advise on the many problems concerned in the diagnosis and over-all care of the child with a disability.

The definition quoted of a handicapped child is a good one: "Any child with a physical, mental or emotional problem which interferes with normal growth and development". Thus, while there are excellent sections on children affected by poliomyelitis, cerebral palsy and muscular dystrophy, there are equally good sections dealing with such conditions as congenital heart defect, mongolism, rheumatic fever, nephrosis and cystic fibrosis, and with disorders of speech, vision and hearing. There is an interesting chapter on counselling in medical genetics.

The changes brought about by modern methods of treatment are such that the longer-stay and more chronic conditions of child illness occupy much more of the work

of the paediatrician than previously. He must, therefore, be prepared to give time to the educational, social and environmental problems of his small patients. From this book he will gain much information relating to the well-being of the whole child, which will be of great service to him.

The authors of the various chapters, including those non-medical authors dealing with education, social service and educational psychology, are leaders in their own particular field; they write clearly and concisely. The editing is good, and altogether this is a valuable and necessary compendium for those with the responsibility for the care of children. The basis of this book has been to give all possible information to help reach the objective of good care for the handicapped child—

To see that every child is cared for in such a manner as to assure recovery when possible, to secure the greatest degree of improvement when complete recovery is not possible, and to help the child to make satisfactory adjustment to society, to his family and to his environment.

Epidemic Diseases. By A. H. Gale; 1959. Mitcham, Victoria: Penguin Books Pty. Ltd. 7½" x 4½", pp. 160, with 21 illustrations. Price: 5s. 6d.

"IN medicine, perhaps more than in any other subject, ideas and nomenclature have changed enormously even in the last seventy years, and almost out of recognition between 1948 and 1950." This renders all the more difficult the task of the historian tracing the history of disease. In this book, which deals with the historical aspects of viral and bacterial diseases of man which have ravaged England over the last five hundred years, a wide variety of disease entities is discussed, the accent being on serious illnesses rather than those, such as chicken-pox, which have led relatively blameless lives and have little recorded history.

After a brief introduction describing immunity, vaccines and mutation for the general reader, the author examines the sources of his material, giving the fascinating history of the old Bills of Mortality (and even appending one in its entirety) up to the establishment of the General Register Office in 1837 with the subsequent complete and reliable records of births and deaths.

The author is well equipped to inform us on epidemiology, having been lecturer in the subject at Bristol University up till his death in 1956, in which capacity he carried on extensive research into epidemiology of infections of childhood. He writes interestingly and well, although with perhaps too much detail for the general reader. The medical man will absorb it with delight. The book's one failing, we consider, is its comparative obsolescence, for the years since 1952, the most recent date given, have seen major advances in the poliomyelitis and influenza stories, of which this work gives not a hint. But perhaps this is unfair, and we applaud this new addition to the Pelican Medical Series.

Medical Radiographic Technique. Prepared by Technical Service X-Ray Department, General Electric Company, under the original editorial supervision of the late Glenn W. Files; revision by William L. Bloom, Jr., John L. Hollenbach, R.T., James A. Morgan, R.T., and John B. Thomas, R.T.; second edition; 1959. Oxford: Blackwell Scientific Publications. 10" x 7", pp. 400, with many illustrations. Price: 82s. 6d. (English).

THIS book is purely a book for technicians. A number of similar publications exist, and naturally, originality in these works is difficult.

There are introductory chapters on the theories of radiation and their practical application. Very good chapters are presented with discussion of the various circuits, to give the technician a greater familiarity with the electro-technological side of his profession. This is put in a way to be readily understood, and simple language helps a better and swifter grasp of the essentials.

The choice of equipment is wisely left to other people, but the establishment and conduct of a dark room, which are well within the province of the technician, are fairly well discussed.

There is a good chapter on the essentials of tomography, and considerable space is given to an anatomical review which, though elementary, covers the subject to a standard which should be quite adequate.

The latter part of the book presents very little that is new in technical work, and is mainly a reiteration of former publications; but, of course, due regard has been paid to recent advances and serial radiography, particularly for angio-cardiography and cerebral aortography.

The book is good in its coverage of the subject, and can be recommended with safety as a book of reference for technical assistants.

Grundriss der Physiologischen Chemie für Veterinärmediziner, Humanmediziner und Biologen. By M. Schenk, M.D., D.Phil., and E. Kolb; 1959. Jena: Veb Gustav Fischer Verlag. 9½" x 6¾", pp. 347, with illustrations. Price: 23.80 DM.

IN such a rapidly expanding subject as biochemistry, it is difficult to present a textbook balanced so as to meet equally the needs of biological, veterinary and medical students. However, this has been well accomplished in the third edition of the book under review; the 300-odd closely-packed quarto pages contain a thorough treatment of the groundwork of the subject.

The book contains no original references, or even a chosen bibliographical summary, which would have increased its value; but a useful stimulant to the student is to be found in an appendix of 535 questions. There are few omissions in the text, though one would have liked to see some reference to the hydroxyindoles (serotonin, argentaffin, etc.) and at least a mention of the important role of the liver in the conjugation of bilirubin with glucuronic acid.

This is an excellent textbook in many ways. A larger and clearer type would do much to improve its appearance.

Cell and Tissue Culture. By John Paul, M.B., Ch.B., Ph.D., M.R.C.P.Ed.; 1959. Edinburgh and London: E. & S. Livingstone, Limited. 8½" x 5½", pp. 272, with 40 illustrations and 16 tables. Price: 30s. (English).

This book, according to the preface, is an attempt to provide an up-to-date account of the techniques and applications of tissue culture. It is divided into four parts. The first part is concerned with the structural organization of cells, and gives brief descriptions of their metabolism and nutritional requirements. The second part deals with apparatus and laboratory design. The third part describes the various techniques used in tissue and organ culture while the morphology of explants is the main concern of the fourth part. The planning of experiments is briefly discussed, together with the technical methods to be applied. There is a brief account of the scope of tissue culture and virology. In general, this book is concise, readable and easily understood. It should prove useful for anyone wishing to enter the field of tissue culture.

A Textbook of Surgical Physiology. By R. Ainslie Jamieson, M.B., F.R.C.S.Ed., and Andrew W. Kay, M.D., Ch.M., F.R.C.S.Ed., F.R.F.P.S.G.; 1959. Edinburgh and London: E. & S. Livingstone Limited. 9½" x 6", pp. 632, with 186 illustrations. Price: 55s.

THERE are many who hold to the view that we have, for far too long, afforded to anatomy a place of authority in the training of the young surgeon. Certainly our American cousins seem in no way to have suffered from long since departing from this traditional practice. The influence of the Scottish schools has been particularly strong in its rigid insistence on an exacting apprenticeship in topographical anatomy as a primary requirement for any graduate aspiring to become a surgical consultant. It is all the more surprising and all the more heartening (if one looks at things this way) to welcome this new text, which comes from the Glasgow school (Mr. Kay has since been called to the Chair of Surgery in Sheffield).

If there is any surgeon who is still reluctant to admit that there is a place for the closer study of physiology in the course of surgical training, he should read this volume from cover to cover. It is, of course, physiology qualified by "surgical", and it is inevitable, as the authors freely admit in the preface, that they should on occasions stray into the fields of physiology and of clinical surgery as well. It is, however, in our view, all the better for this, and as one reads, there is never any feeling of remoteness from things practical; rather it seems that there is a patient in the room and a bright young surgeon busily turning over the pages.

The young man reading for his primary Fellowship will welcome this publication with enthusiasm; but it would be a pity indeed if its reading public was thus restricted. It could, with great profit, serve as the basis for the teaching of every clinical instructor at undergraduate level, and even the most experienced of the older surgeons would find pleasure and enlightenment from a few hours spent with it as reasonably light fireside reading.

It seems proper, in reviewing this book, to pay more attention to its purpose and its scope than to an analysis of its text in detail, for, as far as we are aware, it represents something new in British writing. It is inevitable that in its content there will be evident an emphasis which reflects the primary interests of its authors; but there is in every section such a display of reasonableness and of good judgement that there is no room for criticism. The material is attractively presented, but the cost is for these days a moderate one.

Any book which deals with the advancing edge of a subject dates quickly, but no prospective buyer should be deterred on this account. We shall be surprised if it does not progress from strength to strength with new editions; but the immediate dividend from its speedy purchase will be, for everyone, a satisfying one.

Kurzer Atlas für das klinische Laboratorium. By Dr. med. Eberhard Goetze; 1959. Jena: Veb Gustav Fischer Verlag. Sydney: Angus & Robertson, Limited. 9½" x 6¾", pp. 46, with many illustrations. Price: DM 12.75.

THIS small atlas has been written as a supplement to a textbook of laboratory methods entitled "*Einrichtung und Methoden des klinischen Laboratoriums*". The author, Dr. Eberhard Goetze, is "Professor mit Lehrstuhl für Pathologische Physiologie; Direktor des Institutes für Pathologische Physiologie der Friedrich-Schiller-Universität Jena"; this book is designed as a "handy atlas" for medical students who are learning clinical pathology. It includes a series of colour pictures of the cells of normal blood and bone-marrow; seven pages of photomicrographs in colour of the blood and bone-marrow in disease, and a series of pictures of sediments and other structures seen in the microscopic examination of urine and faeces. The colour photographs and most of the other illustrations are of good average quality. While it is true, as the author points out, that a small atlas of this type may be useful to medical students, it is not to be compared in usefulness to the many good handbooks of clinical pathology which are available, and which have, as a rule, better and more comprehensive illustrations and the great advantage of systematic descriptions. However, the book is intended as a supplement to a larger textbook. Only a very superficial "penny in the slot" sort of knowledge could be gained from the use of this small atlas without a larger textbook.

Soil, Grass and Cancer: Health of Animals and Men is Linked to the Mineral Balance of the Soil. By André Voisin, translated from the French by Catherine T. M. Herriot and Dr. Henry Kennedy; 1959. London: Crosby Lockwood & Son, Limited. 8½" x 5½", pp. 320, with 16 illustrations. Price: 30s. (English).

A GREAT deal of interest is being taken at the present time in the effects in man and animals of deficiencies in the diet of what have been called trace elements, such as copper, cobalt and molybdenum. The picture is quite clear with farm animals. If the soil on which the pasture is grown is deficient in copper, sheep fed on the pasture will show certain definite symptoms; if it is deficient in cobalt, they will show other distinctive symptoms. The signs are not so clear with man for a variety of reasons. A main reason is that man's food does not, as a rule, come from only one farm field, but generally from widely scattered sources. André Voisin, who has for many years been a prominent advocate of the ill effects of mineral deficiencies, has produced a book, "Soil, Grass and Cancer", in which he discusses at great length how the health of animals and men is linked to the mineral balance of the soil. This has been translated from the French by C. T. M. Herriot and H. Kennedy.

Although one must disagree with many of the interpretations and conclusions, it is an interesting book. More than half of the book is taken up in discussing the effects of deficiencies in the soil on animals eating the pasture grown on the soil and the supposed reasons for the effects in the animals. These may be direct effects of mineral deficiencies on the animal, or effects of deficiencies on the pasture causing it—for example, to produce proteins deficient in certain amino acids. This part is particularly interesting provided that one reads it critically. The author has read very widely—the bibliography gives 428 references, many of them books or long reviews. All is grist that comes to the author's mill. If he has read an article by an obscure author in an obscure journal and the conclusions are favourable to his point of view, he accepts them quite uncritically.

There is considerable discussion on the relation of copper deficiency to the catalase content of the cells and to the

effect of deficient catalase. The author makes much of the so-called mobilization of copper in antimicrobial defence. The effects of mineral deficiency in man are discussed mainly in relation to deficiency of copper, although iodine is also considered at length. The theory that cancer and virus diseases are closely related in man to copper deficiency is discussed at some length, and it is here particularly that one finds the acceptance of very doubtful conclusions from experiments. No acceptable evidence is presented that there is ever deficiency in copper in the diet of sufferers from cancer.

Much can be learnt from reading this book but one must keep a very critical mind in so doing. It is, indeed, probable that few, if any, trained scientists would accept the conclusions.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Work of WHO 1959: Annual Report of the Director-General to the World Health Assembly and the United Nations", Official Records of the World Health Organization No. 98, March, 1960. Geneva: World Health Organization. 11" x 8½", pp. 283, with illustrations. Price: 10s. (English).

"A Way of Life", by Sir William Osler; 1960. New York: Dover Publications, Inc. 8½" x 3½", pp. 30. Price: Gratis to teachers of medicine, medical schools, hospitals and medical libraries.

"Health Service, Society, and Medicine: Present Day Health Services in Their Relation to Medical Science and Social Structures", by Karl Evang, M.D.; 1960. London, New York and Toronto: Oxford University Press. 8½" x 5½", pp. 180. Price: 34s. 9d.

"Inheritance of Glioma: The Genetic Aspects of Cerebral Glioma and Its Relation to Status Dysraphicus", by H. J. Van Der Wiel; 1960. Amsterdam, London, New York and Princeton: Elsevier Publishing Company. 9" x 6", pp. 284. Price: 63s. (English).

"Local Health Service: Third Report of the Expert Committee on Public Health Administration", World Health Organization, Technical Report Series, No. 194; 1960. Geneva: World Health Organization. 9½" x 6½", pp. 49. Price: 3s. 6d. (English).

"Medische Ethiek En Gedragseer", by Derde Druk; 1959. Amsterdam: Koninklijke Nederlandsche Maatschappij Tot Bevoororderen Der Geneeskunst. 7" x 4½", pp. 304. Price: Not stated.

"The Principles and Practice of Medicine: A Textbook for Students and Doctors", by Sir Stanley Davidson, B.A., Cantab., M.D., F.R.C.P., Edin., F.R.C.P., Lond., M.D., Oslo, F.R.S., Edin.; Fifth edition, 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" x 5", pp. 1128 with many illustrations. Price: 35s. (English).

"Pathology of Infancy and Childhood", by Agnes R. Macgregor, M.D., F.R.C.P.E., F.R.C.O.G.; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" x 5½", pp. 640, with many illustrations. Price: 75s. net (English).

"Annual Review of Medicine", edited by David A. Ryland and assisted by William P. Creger; Volume 11, 1960. Palo Alto, California: Annual Reviews, Inc. 8½" x 6", pp. 464. Price: \$7.50.

"Guide to Hygiene and Sanitation in Aviation", World Health Organization, 1960. Geneva: World Health Organization. 9½" x 6½", pp. 51. Price: 3s. 6d. (English).

"Word and Object", by William Van Orman Quine; 1960. New York and London: John Wiley & Sons, Inc., and The Technology Press of The Massachusetts Institute of Technology. 9" x 5½", pp. 312. Price: \$5.50.

"Physiology of Prematurity: Transactions of the Fourth Conference, March 25, 26 and 27, 1959, Princeton, N.J.", edited by Jonathan T. Lanman, M.D.; 1959. New York: Sponsored by the Josiah Macy, Jr. Foundation. 9" x 6", pp. 188. Price: \$4.50.

"A Clinical and Genetic-Statistical Study of Schizophrenia and Low-Grade Mental Deficiency in a Large Swedish Rural Population", by Bertil Hallgren and Torsten Sjogren, *Acta Psychiatrica et Neurologica Scandinavica*, Supplement 140, Volume 35; 1959. Copenhagen: Ejnar Munksgaard. 9½" x 6½", pp. 68. Price: 25 Swedish Crowns.

"Leptospirosis: A Bibliography of Literature 1957-1959", compiled by Dorothy Bocker, M.D.; 1959. Washington, D.C.: U.S. Department of Health, Education, and Welfare. 10½" x 8", pp. 46. Gratis.

"Expert Committee on Biological Standardization: Thirteenth Report", World Health Organization, Technical Report Series No. 187; 1960. Geneva: World Health Organization. 9½" x 6½", pp. 47. Price: 1s. 9d. (English).

"Insecticide Resistance and Vector Control: Tenth Report of the Expert Committee on Insecticides", World Health Organization, Technical Report Series, No. 191; 1960. Geneva: World Health Organization. 9½" x 6½", pp. 98. Price: 3s. 6d. (English).

"The Pragmatic Conception of Justice: University of California Publications in Philosophy", by Raymond Jaffe; Volume 34, 1960. Berkeley and Los Angeles: University of California Press, and London: Cambridge University Press. 9½" x 6", pp. 128. Price: Not stated.

"Antibiotics Annual 1959-1960; Seventh Annual Symposium on Antibiotics", edited by Henry Welch, Ph.D. and Felix Marti-Ibanez; 1960. New York: Antibiotics, Inc. and Interscience Publishers, Inc. 10" x 6½", pp. 1054 with illustrations. Price: \$15.00.

"Annual Epidemiological and Vital Statistics 1956", World Health Organization; 1959. Bilingual edition (French and English). Geneva: World Health Organization. 11" x 8½", pp. 705. Price: £3.

"Medische Ethiek En Gedragseer", by Derde Druk; 1960. Koninklijke Nederlandsche Maatschappij Tot Bevoororderen Der Geneeskunst. 7" x 4½", pp. 304. Price: Not stated.

"Clinical Tropical Diseases", by A. R. D. Adams and B. G. Maegraith; Second Edition, 1960. Oxford: Blackwell Scientific Publications. 8½" x 5½", pp. 552, with illustrations. Price: 52s. 6d. (English).

"The Origins of Love and Hate", by Ian D. Suttie, with a Preface by Dr. J. A. Hadfield; 1960. Mitcham, Victoria: Penguin Books. 7" x 4½", pp. 240. Price: 5s. 6d.

"Production of Hypercholesterolemia and Atherosclerosis in Rabbits by Feeding Different Fats without Supplementary Cholesterol", by Gerhard Wigand, Supplementum 351; 1959. Lund: Acta Medical Scandinavica. 9½" x 7", pp. 92, with 20 illustrations. Price: Subscription.

"Adrenocorticotropins and their Use", by H. F. West, Supplementum 352; 1960. Stockholm: Acta Medica Scandinavica. 9½" x 7", pp. 40, with many figures. Price: Subscription.

"Microchemical Methods for Blood Analysis", by Wendell T. Caraway, Ph.D.; 1960. Illinois: Charles C. Thomas. 9" x 5½", pp. 128. Price: 42s. (English).

"Atlas of Anatomy and Surgical Approaches in Orthopaedic Surgery—Upper Extremity", by Rodolfo Cosentino, M.D., with a Preface by Arthur Steindler; 1960. Illinois, U.S.A.: Charles C. Thomas, and Oxford: Blackwell Scientific Publications Ltd. 11" x 8½", pp. 208. Price: 84s. (English).

"The Diagnostic Value of Conventional Radiological Examination of the Heart in Adults", by Per Amundsen, Supplement 181; 1959. Oslo: Acta Radiologica. 9½" x 7", pp. 100 with 13 illustrations and 32 tables. Price: Sw.Kr. 20.

"Acoustico-Cineradiographic Analysis Considerations: with Especial Reference to Certain Consonantal Complexes", by H. M. Truby, Supplement 182; 1959. Stockholm: Acta Radiologica. 9½" x 7", pp. 227 with 126 illustrations. Price: Sw.Kr. 35.

"Angiographic Studies of the Anatomy of Single and Multiple Renal Arteries", by Erik Boijesen, Supplement 183; 1959. Stockholm: Acta Radiologica. 9½" x 7", pp. 135 with 56 illustrations and 16 tables. Price: Sw.Kr. 30.

"A Technique for Destruction of the Hypophysis Using Y⁹⁰ Spheres: A Radiologic, Endocrine and Histologic Study", by Gustaf Notter, Supplement 184; 1959. Stockholm: Acta Radiologica. 9½" x 7", pp. 128 with 64 illustrations and 7 extensive tables. Price: Sw.Kr. 37.

"The Subarachnoid Cisterns: An Anatomic and Roentgenologic Study", by Bengt Lillequist, Supplement 185; 1959. Stockholm: Acta Radiologica. 9½" x 7", pp. 108 with 86 illustrations. Price: Sw.Kr. 35.

"Pontine Angle Tumour: Encephalographic Appearances", by Bengt Lillequist, Supplement 186; 1959. Stockholm: Acta Radiologica. 9½" x 7", pp. 96 with 67 illustrations. Price: Sw.Kr. 30.

"On the Design, Physical Properties and Practical Application of Small Condenser Ionization Chambers", by Holger Skoldborn, Supplement 187; 1959. Stockholm: Acta Radiologica. 9½" x 7", pp. 108 with 42 illustrations and 9 tables. Price: Sw.Kr. 30.

"Clinical Endocrinology, I", edited by Edwin B. Astwood, M.D.; 1960. New York and London: Grune & Stratton. 9" x 5½", pp. 745, with many illustrations. Price: \$18.75.

"Rose and Carless: Manual of Surgery", consulting editor, Sir Cecil Wakeley, Bt., K.B.E., C.B.; editors, Michael Harmer and Selwyn Taylor, assisted by fifteen contributors; Nineteenth Edition; 1960. London: Baillière, Tindall and Cox. 9½" x 6", pp. 1408 with many illustrations. Price: 84s. (English).

The Medical Journal of Australia

SATURDAY, JULY 16, 1960.

COME TO NEW ZEALAND.

REMARKABLY few Australians have been to New Zealand, although it is our nearest sister Dominion, bound with us by very close ties, and is at the same time a tourist country of world renown. It is not as far away as it seems to be and is in fact closer to the eastern coast of Australia than is Australia's western coast. Medically Australia and New Zealand are very closely linked. Our two senior Royal Colleges are both Australasian, as are a number of our specialist groups, and we belong to the same British Medical Association. On a national level the bond implicit in the word ANZAC is imperishable.

Early next year Australian doctors will have a unique opportunity to visit New Zealand—the 129th Annual Meeting of the British Medical Association, which is to be held in Auckland from February 6 to 10, 1961, in conjunction with the Biennial Conference of the New Zealand Branch. It may well be the last Annual Meeting of the B.M.A. to be held before Australia forms its own medical association and so the last occasion when we can share this bond with our colleagues not only from New Zealand but also from the United Kingdom, which will be well represented. The programme of the meeting, which is published elsewhere in this issue (see page 111) is attractive from both the scientific and the social points of view, and no effort is being spared to make it as good as possible. Plenary sessions will be devoted to the following subjects: "Maintaining the Health of the Middle-Aged Executive", "General Surgical, Medical and Psychological Problems of Pregnancy", "Chemotherapy in Cancer", "Iso-immunization: A New Concept of Disease", "Mental Health in the Community". Round table conferences will be held on thyroid disease, the present position of steroid therapy and ulcerative colitis. The social programme will include an afternoon launching on the Waitemata Harbour for conference members and their wives, a late afternoon reception by the President and members of the Auckland Division, the Annual Dinner and the Conference Ball, as well as private entertainment and excursions.

Our New Zealand colleagues have opened their doors wide in a warm invitation to Australian doctors and their wives for this occasion and will be most disappointed if the response is poor. Their main problem at the moment is to know how many visitors are likely to attend as most arrangements must be made far in advance, especially those for accommodation. The meeting, it must be remembered, is right at the height of the tourist season. Of particular interest and attractiveness is an invitation issued by the Southland Division of the B.M.A. to overseas

visitors. They have arranged a four-day tour, commencing on Thursday, February 16, to visit Fjordland. The Southland Division will arrange all accommodation and a number of tours, including the Milford Track, as well as excursions on the lakes and car trips around the valleys of Fjordland. In view of the need to make bookings, they are anxious to know if any Australians would be interested in this invitation. In addition, hospitality has been arranged in all centres in New Zealand, and Australian visitors are assured of a very warm welcome both at the Conference and subsequently when they tour the country. Our New Zealand colleagues have emphasized that the sooner they can get a clear idea of the numbers coming, the better the arrangements for accommodation will be, and this applies as well to any trips that visitors may care to make either before or after the Conference.

So far only 24 applications have been received from Australia. This surely represents only a fraction of the Australian doctors who could go and no doubt intend to go. Application forms are obtainable from the Branch offices of the B.M.A. in each State. The sooner they are filled in and sent by air mail to New Zealand the better for everyone. This opportunity is too good to miss.

PRESERVATION OF MEDICAL RECORDS.

Not long ago the original minute book of one of Australia's oldest and most important hospitals was rescued from the incinerator only by the thoughtfulness of a hospital attendant who might not have been expected to have the slightest interest in such matters. This minute book is well over a century old and contains the minutes of the meetings which led up to the foundation of the hospital, as well as much else relating to the hospital's beginnings. It is an invaluable historical document, passed over by everyone who might reasonably have been expected to appreciate its importance.

How many more such documents are being destroyed from day to day it is impossible to say, but this is not likely to be an isolated instance. We are not a very history-minded people and discard with gay abandon any records which appear to have no immediate usefulness. This is all the more important since the history of European civilization in Australia is compassed in quite a short period, and it should be possible for it to be fully documented. The history of medicine in Australia has not yet been written or even planned in any comprehensive way, and it would be a tragedy if the basic documents were lost before they had even been consulted.

The British Records Association has recently published a memorandum¹ which deals with the presentation of medical records. It warrants the fullest publicity. Some of the details of how records may be dealt with apply in essence to the United Kingdom, but there is much sound advice on what documents should be preserved—some of them quite unlikely by uninformed standards. The memorandum lists the following as the kind of record to be searched for:

Foundation deeds, statutes and rules of medical societies and institutions, medical charities and dispensaries, and medical schools.

¹ *Lancet*, 1960, 1:379 (February 13).

Minute books of governing bodies and committees.

Ledgers and main accounting records.

Annual reports and balance sheets.

Registers, such as those of students undergoing training or of patients admitted to hospital, where more than the patient's name is given.

Letters written by medical men which may be of professional or personal interest; (the former may prescribe a course of treatment, give an opinion on a case or throw light on medical education; the latter may have bibliographical value).

Lecture notes, which may provide the only source of information for lectures of distinguished physicians and surgeons and give some indication of the state of knowledge of the time; and other students' notes.

Licences (including letters testimonial) to practise medicine generally or in one of its branches.

Partnership agreements.

Account books and ledgers, which may contain information about the size of a doctor's practice, professional fees, the cost of drugs, etc.

Case books and medical diaries.

Prescription books.

Copies of this memorandum, which *The Lancet* prints in full, may also be obtained free from the Secretary, Records Preservation Section, British Records Association, The Charterhouse, London, E.C.1. It would be a good idea if a copy of it could be put into the hands of all who are responsible for the handling of records in hospitals and other institutions, medical organizations of all kinds, medical schools and libraries. Even the private practitioner and those who have the responsibility of dealing with private practice records after a doctor's death need to bear the matter in mind. If there is doubt about any documents, advice should be sought. Apart from the public libraries in each State, the Royal Australasian College of Surgeons in Melbourne has a historical library and The Royal Australasian College of Physicians in Sydney is embarking on the development of one. In particular, the Section of Medical History of the Victorian Branch of the B.M.A. is actively interested in the preservation of all material of medical historical importance; a letter of inquiry to the honorary secretary of the Section, addressed to 426 Albert Street, East Melbourne, C.2, would undoubtedly elicit a helpful response.

Current Comment.

INFANT MORTALITY.

A STATISTICAL REPORT¹ on infant mortality, just published by the World Health Organization, shows that the lowest figures yet recorded have been reached in a number of countries. Sweden shows 16 deaths per 1000 live births, the Netherlands and Iceland 17, New Zealand 19, Australia 20 and Switzerland 22; all these figures apply to the year 1958. No foolproof comparisons can be made for all countries because of differences in definitions, in procedures, and in completeness of registration. However, if it is assumed that the infant mortality rate is traditionally regarded as a good measure of an area or country's sanitary situation, the figures provided by the report, which cover 38 areas around the world from 1901 to 1958, are worthy of interest. They show clearly, for instance, that the rate of improvement is far from being the same everywhere. Expression of the 1957 infant mortality rate as a percentage of the 1921-1925 rate (at which time a general decrease became apparent throughout the world) shows that Malta was down at only 15%, Singapore at 18%,

Hawaii at 20%, Czechoslovakia at 21% and the Netherlands at 24%. On the other hand, countries like Guatemala (96%), Uruguay (85%), Yugoslavia (70%), El Salvador (64%), Portugal (60%) and British Honduras (59%) reported a much slower rate of progress.

Infant mortality rates are usually divided into two groups—deaths that occur in the first four weeks of life, and those that occur later, up to the end of the first year. It is in the latter category that the greatest over-all improvement (between 60% and 70% in many countries) can be observed, and this is considered to be due to the general improvement in the environment of the child. Another section of the report deals with mortality among children from one to nine years of age for the period 1955-1957. It covers fewer countries, but shows clearly that there is a change in the relative importance of illness (infectious and other diseases) on the one hand, and violent deaths (accidents and poisoning) on the other.

Throughout the age groups, the place of infections is relatively minor in almost all the countries under study. During the three years, for instance, there were no deaths from diphtheria in Denmark, while malignant neoplasms (including leukaemias) accounted for 190 deaths. Even in Italy, where there was a significant amount of diphtheria (a total of 1481 deaths in the period 1954-1956) there were nevertheless more deaths from malignant neoplasms (1999). The situation is, however, different in countries still in the process of development, which have to cope with the problem of infectious diseases.

In certain areas, violent (accidental) deaths outnumbered all diseases put together. Male deaths in this class for the five to nine years age group were 62.2% of all deaths in Norway during the years under study. Sweden (52.2%) and Canada (55%) show the same situation. Drowning and road accidents appear to be greater hazards for boys than for girls, both being protected from childhood illnesses by successful preventive campaigns. Girls are perhaps better watched or less adventurous, since in none of the age groups studies were accidents the major cause of death. This is particularly apparent in Norway, where in the five to nine years age group two-thirds of the male deaths were due to violence, while two-thirds of female deaths were still due to disease.

CHILDHOOD SCHIZOPHRENIA.

It has been said that the schizophrenic is incompletely equipped to cross the bridge between childhood and maturity (H. Wilson, 1957²), and that this is why schizophrenia characteristically makes its appearance in adolescence or in early adult life. Schizophrenia in childhood is therefore almost by definition a rather distinct entity, and it appears that a considerable difference of opinion surrounds this diagnosis. R. R. Koegler and E. G. Colbert² have recently discussed the subject in the light of an intensive study of 34 children with a diagnosis of schizophrenia, and make a plea for the earlier recognition of the condition so that treatment may be instituted with more hope of success. They state that hitherto delay in diagnosis has been usual and that the many years for which the condition has gone unrecognized often render treatment impracticable; 15 years ago many schizophrenic children were considered to be mentally retarded or to be suffering from organic brain disease, but the clinical importance of childhood schizophrenia has in recent years been recognized to an increasing extent. In the view of Koegler and Colbert this is a crippling mental disease of unknown aetiology, which in a large proportion of cases makes its appearance before the age of five years. In some cases symptoms appear within the first few months of life, and this is followed by progressive deterioration. However, an initial period of relatively normal development is more usual, followed by fairly sudden regression between the ages of one and three years. The subjects of Koegler and Colbert's study were 34 children from a State hospital unit,

¹ *Brit. med. J.*, 1957, 1: 1502 (June 30).

² *J. Amer. med. Ass.*, 1959, 171: 1045 (October 24).

¹ *Epidem. Vital Statist. Rep.*, 1960, 13: 41.

who had been referred to hospital with a diagnosis of childhood schizophrenia (in which Koegler and Colbert concurred) by various psychiatrists. In all of them the disorder had begun before the age of five years. The study was conducted by means of a questionnaire to the parents in an attempt to ascertain the nature of the initial signs and symptoms. Many significant differences were found when the answers were compared with the answers to the same questions about children with behaviour disorders. Koegler and Colbert state that their study tends to confirm the belief that there is evidence of neurophysiological differences between schizophrenic and non-schizophrenic children. Diagnosis depends mainly on developmental history and clinical observation of the neurophysiological state, with attention to the degree of socialization and the play pattern. Results of psychological testing were found to be disappointing, and are almost completely valueless with patients under five years old. Koegler and Colbert state that the genesis of childhood schizophrenia is not sufficiently understood for there to be any certainty about the best method of treating the condition. However, in one reported series which they quote, a follow-up study has shown that two-thirds of the children had left hospital and were doing fairly well in their teens and later. They conclude with the hope that increased awareness of the condition by family doctors and paediatricians will result in earlier treatment, so that many more of these children will become useful citizens.

It should, however, be noted that this is only one side of the picture. In a letter commenting on Koegler and Colbert's paper, D. D. Jackson³ points out that many authorities do not accept a primarily physiological basis for childhood schizophrenia, that one had found no evidence for genetic factors in these children, and that another, after 10 years of intensive research, concluded that childhood schizophrenia had a psychological aetiology. (Koegler and Colbert have commented on the distress caused in some cases by parental feelings of guilt, due to what was, in their opinion, misleading emphasis on the causative role of psychological factors, such as parental rejection, etc.) Elsewhere, H. L. Mosse⁴ has expressed his concern at the enormous increase in the frequency of the diagnosis of childhood schizophrenia, stating that in the United States it is at present a fashionable and much abused diagnosis. After a study of 60 patients with a diagnosis of childhood schizophrenia studied at the Lafargue Clinic, New York, he concluded that the diagnosis in practically all of them was wrong. The group included patients with behaviour problems, patients with organic disorders and psychopaths. Mosse discusses some of the reasons for these errors in diagnosis, and has no difficulty in showing the enormous harm which can arise from such mistakes. One of his patients, a boy, aged nine years, had been subjected to 20 electroconvulsive treatments, and he states that elsewhere children of all ages had been subjected to lobotomy on the same basis. It seems clear that the question of childhood schizophrenia is a thorny one, with pitfalls on either hand.

SILICONES IN MEDICINE AND SURGERY.

TEN years ago the possible and accepted uses of silicones in medicine and surgery were reviewed in these columns.⁵ The subject was then in its early stages of development, but it was apparent that a good deal could be done with these extremely inert and tractable substances. Their virtues lie in their physical properties: with their low surface tension they spread easily; they can provide a surface film which keeps tacky materials from sticking together; they are very repellent to liquid water although they transmit water vapour; because of their chemical inertness they are said not to be attacked by enzymes or to support bacterial growth. Fields in which these prop-

erties have been found useful include dermatology, instrument sterilization, veterinary practice, especially in the management of cattle bloat, the internal coating of tubing to carry blood, the preparation (in the form of silicone rubber) of tubing and various appliances used in modern surgery. Many other uses have been suggested; some have been tried without success, others await adequate trial. It is clear, however, that the properties of silicones present attractive possibilities, especially in the increasingly complex gadgetry demanded by surgeons today. With this in mind the Dow Corning Corporation in America has formed the Dow Corning Center for Aid in Medical Research. The purpose of this centre is to serve the medical profession on a non-profit basis by (a) providing technical aid in the use of silicones in medicine and surgery, (b) acting as a clearing house for information about medical uses of silicones and (c) cooperating in research in organosilicon chemistry in relation to the human body. The Dow Corning Corporation is of course interested commercially in the silicones, but the new centre has been established as a unit separate from the Corporation's commercial activities although allied with its research department. The director of the centre is Dr. Rob Roy McGregor, who has been working in the field of organosilicon chemistry for over 20 years and has done a good deal of pioneer research. The resources of the centre are offered free to members of the medical profession, and inquiries will be cordially welcomed. They should be directed to the Dow Corning Centre for Aid in Medical Research, Midland, Michigan, U.S.A. It is emphasized that all information about medical research will be held in strict confidence unless specific permission for publication is granted, and that officers of the centre cannot offer advice concerning medical matters or help secure financial aid for medical research products. Otherwise they place their services and those of their associates at the disposal of the medical profession.

RHEUMATIC FEVER AND EGG YOLK.

Few medical conditions of childhood have received more attention than rheumatic fever, and yet there is still great uncertainty about some aspects of the disease. There is wide agreement on many points. Typically, an attack of rheumatic fever follows an acute infection with a β haemolytic streptococcus. Its incidence is very much higher among the low-income groups in most communities. There is considerable evidence of a genetically determined susceptibility. Beyond this point we are on uncertain ground. Some are content to say that the incidence is higher because of over-crowded conditions with more frequent exposure to infection. The possibility that dietetic factors may be involved has also been seriously examined by a number of authors. Professor A. F. Coburn of New York Medical College has been prominent among these, and has recently marshalled the evidence in support of the suggestion that egg yolk may play a vital role in this respect, in an article¹ which commands attention. Coburn has no difficulty in showing that most children who developed rheumatic fever before puberty had had inadequate diets in childhood, including low egg consumption. He is also able to cite four different trials in which the provision of egg supplements of one kind or another to rheumatic children resulted in a marked decrease in the incidence of rheumatic recurrences. Evidence is quoted that the active principle is in the alcohol-soluble fraction of egg-yolk, and an anti-allergic component of this fraction has been isolated; Coburn reports that this is being tested as a dietary supplement among children of the poor in New York City. Enough has been said to indicate very briefly the outlines of a hypothesis which, if substantiated, has implications of far-reaching importance. Coburn concludes by stating that "the underlying biochemical mechanism of the rheumatic state and its relation to nutrition in infancy remain to be determined".

³ *J. Amer. med. Ass.*, 1959, 171: 2246 (December 19).

⁴ *Amer. J. Psychiat.*, 1958, 114: 791 (March).

⁵ *Med. J. Aust.*, 1950, 2: 968 (December 30).

¹ *Lancet*, 1960, 1: 867 (April 16).

Abstracts from Medical Literature.

MEDICINE.

Steroid Therapy and Tuberculosis.

H. SHUBIN *et alii* (*J. Amer. med. Ass.*, August 15, 1959) discuss steroid therapy in tuberculosis. Realizing the possibility of reactivating the disease, the authors used prednisolone in 36 cases of acute and 107 cases of chronic tuberculosis, on the basis that low 17-ketosteroid levels indicated adrenal insufficiency. Streptomycin, isoniazid and PAS were given, and prednisolone was added in divided doses at the rate of 50 mg. per day, being reduced gradually to 15 mg. on the twenty-third day. Marked improvement occurred in many cases. Thirty-two of the patients with acute tuberculosis recovered, including eight suffering from tuberculous meningitis; of those with chronic disease, out of 20 patients with terminal disease who were expected to die, 15 recovered. Six patients with proved sarcoidosis, of whom one also had pulmonary tuberculosis, were included in this study. Because of a possible relationship to tuberculosis, all were put on the prednisolone régime with anti-tuberculosis therapy; there was excellent resolution in all six patients. The authors state that, as chest specialists, they have been seeing an increasing number of patients with reactivated tuberculosis who have received steroids for various diseases. During the previous year they had seen 58 patients in whom active tuberculosis developed during or after steroid therapy without anti-tuberculosis drugs. The authors state that it is not their purpose to discourage the use of steroid therapy, but they urge all physicians using these drugs to investigate the presence of tuberculosis and, if in doubt, to administer simultaneously anti-tuberculosis drugs. The use of steroids in other diseases has produced excellent results, but only when these drugs are used judiciously, that is, in the minimum dosage for the shortest period necessary to obtain the desired results, are complications diminished. The authors conclude by stating that their findings illustrate the paradox that a powerful drug can produce disastrous results when used where indicated, and yet can produce beneficial results when used where contraindicated—but used wisely.

Chloroquine in the Long-Term Treatment of Rheumatoid Arthritis.

J. P. YOUNG (*Ann. intern. Med.*, December, 1959) presents an analysis of results of long-term treatment of rheumatoid arthritis with chloroquine phosphate. Fifty patients received continuous therapy for periods of 18 to 36 months. An individual dose schedule for chloroquine was devised, and thereby side effects from the drug were minimal in number, minor in degree and reversible in character. Initially, a starting dose of 186 mg. per week was well tolerated, and later in the series a starting dose of 125 mg. three times weekly was introduced. The dose is gradually increased as the patient's

tolerance to the drug permits; and when a dose was reached that produced a satisfactory rate of improvement, this dose was maintained indefinitely. The goal of therapy was to obtain some subjective and objective improvement during the first three to six months of treatment while keeping the incidence of side effects at a minimum. A major improvement or complete remission was noted in 85% of the patients, 4% experienced a minor degree of improvement, and in 8% there was no improvement. The improvement was maintained for as long as 36 months without evidence of recurrence of symptoms or weakening of grip strength, such as occurs during long-term steroid treatment. Treatment with chloroquine was followed by a return to normal of sedimentation rates and haematocrits in a much higher percentage of patients than has occurred in series treated solely with anti-inflammatory agents such as steroids, phenylbutazone and aspirin. The improvement in both the sedimentation rates and the haematocrits was found to be highly significant statistically. The rate of bone destruction found in yearly X-ray examinations of the hands appears to be significantly less than was found to occur in groups of patients treated by other methods. The clinical pattern of response follows a sequence similar to that found in patients undergoing a spontaneous remission of arthritis. These differences in the type of improvement following chloroquine therapy make it reasonable to postulate that chloroquine does not act simply as an anti-inflammatory agent, but slowly affects some more basic feature of the disease. Treatment with chloroquine is only one-third to one-half as expensive as treatment with steroids or phenylbutazone. In order to obtain the full benefit of chloroquine treatment, its administration must be continued for more than one and a half years.

Chlorothiazide and Electrolyte Depletion in Chronic Glomerulonephritis.

I. S. FRIEDMAN *et alii* (*A.M.A. Arch. intern. Med.*, January, 1960) describe electrolyte depletion in two patients with chronic glomerulonephritis who had received chlorothiazide in moderate dosages for three weeks. Because of its diuretic and antihypertensive actions, chlorothiazide has been recommended for use in oedematous and hypertensive states, including renal disease. Although this drug is known to cause increased secretion of sodium and potassium, only few untoward clinical reactions have been described during its use. However, since patients with renal insufficiency may have a diminished ability to conserve sodium, potassium and chloride ions, the administration of such a diuretic might accentuate the process of depletion. The records of two cases of chronic glomerulonephritis are presented to emphasize the dangers in the use of chlorothiazide in patients with renal insufficiency. In each case, electrolyte balance studies were carried out, including the measurement of total exchangeable sodium and potassium by the isotope dilution principle. Each patient received chlorothiazide in moderate dosages for three weeks, and both developed increasing

nitrogen retention with clinical manifestations of electrolyte depletion. They responded to a regimen of electrolyte replacement with both clinical and chemical improvement. Isotopic studies confirmed the initial presence of a depletion state, and during the repletion period they showed the return of sodium and potassium to normal levels.

Dietary Fats and Thrombosis.

T. GEILL, P. F. HANSEN AND E. LUND (*Nature (London)*, January 30, 1960) report from Copenhagen that, in order to study the influence of the fat content of food on the occurrence of thrombosis, a group of 133 geriatric patients were given a diet in which butterfat, margarine and lard were replaced by vegetable oils (unhydrogenated corn oil and soya bean oil). The daily intake of vegetable oils was about half the total fat intake (80 grammes). A control group received an ordinary hospital diet, containing about 80 grammes of animal fats daily. In the treated group four cases of thromboembolism occurred, three of them within one month of starting treatment, and one as a complication of bronchial cancer. In the control group 15 cases of thrombosis were observed, including five of myocardial infarction and six of cerebral thrombosis. The authors state that the difference is statistically significant ($t=5.1$) and cannot be interpreted in terms of variations in age, weight and blood pressure between the groups.

The Nephrotic Syndrome.

A. R. SHARPE, JR. AND A. M. UNGER (*A.M.A. Arch. intern. Med.*, November, 1959) present the results of a study of renal biopsy findings in eight adult patients with the nephrotic syndrome, who were treated with prednisone. Diuresis to dryness was observed in every case after the initial course of therapy. To demonstrate the pathological lesion which might be anticipated to respond favourably to prednisone, these patients were studied by renal biopsy. The clinical diagnosis of nephrotic syndrome was based on the pressure of heavy albuminuria, oedema and hypoalbuminaemia. The serum cholesterol was initially elevated in all eight patients, whose ages varied from 24 to 41 years. The nephrotic syndrome has been associated with numerous different aetiologies, but in these patients no definite relationship to any of the aetiologies considered could be demonstrated. After initial examination and baseline studies, the patients were started on prednisone in an arbitrary dosage of 60 mg. per day. The régime was continued until diuresis was complete and urinary protein had decreased to a minimum. No patient completed diuresis in less than 16 days. Unless oedema was increasing or causing excessive discomfort, sodium was not restricted. Three grammes of potassium acetate were given daily in one case, but not in the others. Prophylactic antibiotics were not used routinely. At the completion of intensive prednisone therapy, the patients were started on an interrupted schedule of treatment, being given 60 mg. of prednisone per day for the first three days of each week. This dose was decreased by 5 mg. a day each month so that treatment would be completed by the end

of one year. If relapse occurred, the dose of prednisone was increased to a level sufficient to restabilize the patient. The weight loss after treatment varied from 12 to 57 lb. Proteinemia disappeared in only two patients, but the other six patients were oedema-free and were excreting only small quantities of protein. The serum albumin content increased and the cholesterol level decreased markedly after treatment, but the blood urea nitrogen level remained essentially unchanged. The outstanding pathological lesion in six of these patients as shown by renal biopsy was thickening of the basement membrane, and one had nearly normal biopsy findings. When renal biopsy in the adult nephrotic patient shows nearly normal glomeruli or generalized thickening of the basement membrane, it appears reasonable to institute a regimen of steroid treatment; this should be maintained until diuresis is complete and there has been a reduction in urinary protein to a minimal level. No serious complications occurred in this series, with a dosage of 60 mg. of prednisone daily.

Myocardial Infarction.

H. BLINDER and O. R. SMELIN (*J. Amer. med. Ass.*, November 7, 1959) discuss diagnostic errors due to the electrocardiographic pattern of acute myocardial infarction remaining fixed after the event. Q waves and elevated S-T segments in the precordial leads of the electrocardiogram are commonly interpreted as indicating recent myocardial infarction. The authors report five cases where the above changes were present and were regarded as evidence of recent acute myocardial infarction, and the patients underwent prolonged hospital treatment. These were all elderly patients aged 58 to 69 years. Later electrocardiograms showed that the apparent "acute" changes had persisted for from three months to perhaps eight years. Aneurysm of the left ventricle was found in two of these patients, and in one the wall of the aneurysm was calcified. The authors state that a single electrocardiogram is not enough to establish a diagnosis of recent myocardial infarction because the findings of Q waves and elevated S-T segments in the precordial leads after infarction sometimes persist indefinitely.

Erythrocyte Sedimentation Rate Errors.

V. LORIAN (*Presse méd.*, June 13, 1959) has investigated the chief causes of error in clinical laboratories in the estimation of the erythrocyte sedimentation rate, and reaches the following conclusions: (i) Some of the anticoagulant solutions used—heparin (0.1%) or sodium citrate solution (12%)—make the rate faster by about 20%. (ii) A change in relationship between the volume of sodium citrate solution and of blood will hasten the sedimentation rate if there is too little anticoagulant solution, or slow it if there is too little blood. (iii) Traces of alcohol in the syringe cause a slight reduction in the sedimentation rate. (iv) A sloping position of the tube brings about a remarkable acceleration (70% to 300%) in the sedimentation rate. However, it is not possible to establish a

proportional relationship between the slope of the tube and the acceleration of the sedimentation rate. (v) A high temperature (36° or 37° C.) causes acceleration of the sedimentation rate—as much as 200% in the cases investigated. The author states that, in view of the variations of temperature in the different climates, he considers acceleration of the erythrocyte sedimentation rate by heat the most important and most common cause of errors. It is generally accepted that the estimation is made at about 20° C. He believes that when the estimation is made at another temperature, the actual temperature should be stated as part of the result.

The Kidney in Waldenström's Macroglobulinemia.

P. MICHON *et alii* (*Presse méd.*, June 24, 1959) have studied renal manifestations in Waldenström's macroglobulinemia, on the basis of seven cases of their own and the 200 or so reported in the medical literature. They state that renal abnormalities, which are frequent in this condition, are in all respects similar to those found in multiple myeloma—albuminuria, globulinemia, hyaline casts, Bence Jones proteinuria. There is a resemblance also to the renal stigmata recorded in cryoglobulinemia. The authors suggest a new etiological classification—dysglobulinemic nephropathies. They believe that this new concept has not only a clinical basis, but also an anatomical (glomerulonephrosis) and physio-pathological basis (probable toxic effect of dysglobulinemia). Knowledge of three dysglobulinemic nephropathies in their opinion will make possible a presumptive diagnosis in certain unrecognized cases.

Dangers of Prolonged Anticoagulant Therapy.

W. F. KLESCH *et alii* (*J. Amer. med. Ass.*, January 16, 1960) report the case of a man who took 50 mg. of phenindione twice daily after a myocardial infarction as anticoagulant prophylaxis against possible recurrences. After four years of this therapy he was admitted to the hospital with nausea, vomiting, jaundice and various hemorrhagic manifestations. It became apparent that intercurrent acute hepatitis had potentiated the effect of the anticoagulant. The authors recommend that patients receiving prolonged anticoagulant therapy be watched for the appearance of conditions such as hepatic or renal disease, diabetes and blood dyscrasias. The patient recovered from the hepatitis and discontinuation of the anticoagulant therapy was not followed by any progression of his heart disease.

Renal Function Tests in Chronic Pyelonephritis.

A. KASANEN and H. SALMI (*Acta med. scand.*, volume 165, fascicule 2, 1959) have carried out renal function tests on 350 patients suffering from pyelonephritis to assess their significance in the early diagnosis of chronic pyelonephritis. The authors found that the specific gravity of the morning urine and the haemoglobin value (indicating the presence of renal anaemia) were the most sensitive indicators of incipient renal insufficiency. The next

most sensitive indicator was the phenol-sulphonphthalein test. Glomerular filtration rate and effective renal flow changed only much later. Blood urea and creatinine values did not become elevated until later, after changes had already been observed with other tests.

Remote Stimulation of the Heart by Radiofrequency Transmission.

W. W. L. GLENN *et alii* (*New Engl. J. Med.*, November 5, 1959) were confronted with rapid deterioration of a man aged 73 years who had been in complete heart block for about two years. He had 18 to 30 ventricular contractions per minute and frequent episodes of asystole accompanied by as many as 20 attacks of syncope per day. The authors decided to attempt the stimulation of the heart of this patient by radiofrequency waves transmitted through the integument to a secondary coil embedded beneath the subcutaneous tissue with a wire leading to the left ventricular myocardium. It was hoped to provide prolonged remote control stimulation of the myocardium without danger of infection from wires brought to the exterior and without the discomfort of externally placed electrodes. After insertion of the myocardial electrode and embedding of the secondary coil, the heart responded well to the pacemaker as long as close positioning of the external primary coil and the buried secondary coil was maintained. Stimulation at a rate of 80 times per minute gave regular responses, but at lower rates failed to block the multifocal idioventricular pacemakers which in turn caused unresponsiveness to many stimuli. On the twenty-first post-operative day stimulation of the heart suddenly stopped; probably coincident with this was a short circuit in the radiofrequency pulse generator. Repeated attempts, within the range of stimulus available, to stimulate the heart with a duplicate generator were unsuccessful. The capsule was removed from the subcutaneous pocket under local anaesthesia, and a small collection of creamy material was found around the end of the indifferent silver electrode, though the material was found to be sterile on culture. A few weeks later the patient once again began to have syncopal attacks and died during one of these.

Rheumatoid Spondylitis and Aortic Insufficiency.

O. STORSTEIN and E. WAALER (*Acta med. scand.*, volume 165, fascicule 2, 1959) state that there are two different types of heart lesion in patients with rheumatoid arthritis. Firstly, there may be rheumatoid granulomata in the mitral and aortic rings and cusps, especially in patients with classical peripheral rheumatoid arthritis. Secondly, there is a special type of aortitis with necrosis of the media at the root of the aorta, which occurs in patients with ankylosing spondylitis who may also have arthritis of some of the peripheral joints. Pathologically this rheumatoid aortitis may be quite similar to the better known luetic variety. Histologically the main features are thickening of the vasa vasorum with fibrosis and lymphocytic infiltration of the adventitia. The authors describe two cases of rheumatoid aortitis, and include autopsy studies in one instance.

Brush Up Your Medicine.

THE MANAGEMENT OF ASTHMA IN CHILDHOOD.¹

Specific Therapy.

SPECIFIC aetiological factors should be removed. A detailed allergic history is important and skin tests may be necessary.

Hyposensitization is often helpful in alleviation and gives an ideal opportunity for good general practitioner psychosomatic management.

Psychotherapy occasionally will benefit the parents as well as the patient.

Symptomatic Treatment.

Irreversible emphysema is one of the causes of lack of response to therapy. Energetic early treatment is imperative.

Drug and Other Treatment.

Sympathomimetic Drugs.

Ephedrine.—Ephedrine is the most important and generally the most effective therapeutic agent. It may be combined with a sedative (barbiturate) or with codeine phosphate (gr. 1/6 per dose) as a cough mixture. Ephedrine is a central nervous system stimulant.

Methoxyphenamine.—Methoxyphenamine ("Orthoxine Hydrochloride") is an analogue of ephedrine but with fewer side effects. It is popular and efficacious.

Isoprenaline.—Isoprenaline sulphate ("Neoepinephrine", "Nephenal") is effective, but may produce some palpitation.

Adrenaline.—Adrenaline is the oldest remedy and is still popular. Care should be exercised in giving the correct dosage (subcutaneously): 1 min. to a baby, 7 min. at the end of childhood; this is repeated in 15 minutes if necessary. (N.B.—It is dangerous to give adrenaline by injection to a patient who has recently (within 4 hours) had isoprenaline by mouth or as a spray.)

Aerosol.—Bronchodilators.—Aerosol bronchodilators are sometimes preferred.

Xanthine Derivatives.

Aminophylline.—Aminophylline ("Aminobarb", "Cardiophyllin", "Carine", "Diurophylin", "Glucophylline") in correct dosage is a useful and safe therapeutic agent. Toxic effects (central nervous system stimulation, vomiting, pallor, etc.) may occur with excessive dosage on account of variable absorption from the gastro-intestinal tract and cumulative effects with repeated administration. It can be given orally, intravenously or as a suppository. The latter is often best administered by the parent. The intravenous route should be reserved for severe cases.

Sympathomimetic and xanthine substances used in combination are often superior to a drug from either group used alone.

Iodides.

Iodides are expectorants and assist in liquifying sputum. The dosage is 5 to 15 grains three times a day in milk or fruit juice. Potassium iodide or sodium iodide may be used according to preference and clinical indications. It may be combined with ephedrine.

Caffeine.

Caffeine, used as an elixir of caffeine iodide (B.P.C.), is of value when bronchial infection is associated with asthma.

Steam.

Steam is a good expectorant, a fact often overlooked.

Antihistamines.

Antihistamines are more useful for allergic rhinitis than for bronchospasm and are an excellent vehicle for ephedrine. In the later stages of an attack, with viscid sticky secretion in the bronchi, antihistamines are contraindicated, as they tend to dry the secretion and hinder its removal.

In general they are poor anti-asthmatic drugs.

Sedatives.

Sedatives relieve emotional tension and are, on occasions, more useful than antispasmodics, particularly in the child who panics in an attack.

Sodium phenobarbitone and pethidine hydrochloride (50 mg. dose) are useful in conjunction with antispasmodics.

Asthma may replace anxiety as a psychoneurotic manifestation, especially in children.

Physiotherapy.

Breathing exercises teach the child to use both nose and chest fully and to expire more completely. They are very beneficial in the chronic emphysematous case and assist in removing sticky secretion from the lungs. In status asthmaticus intermittent positive breathing of the inspiratory type may be life-saving.

Oxygen.

Oxygen inhalation is usually necessary only in the severe attack, especially in hypoxic cases.

Fluids.

Fluids are given orally and/or parenterally as required. It is important to watch for dehydration in the severe case with a prolonged attack.

Antibiotics.

If infections initiate asthmatic attacks or are a troublesome complicating factor, it may be necessary to consider antibiotic therapy, but as a general rule these products are rarely required and should be resorted to only after much forethought.

Corticosteroids.

Corticosteroids should be reserved for those cases in which relief cannot be obtained by other measures. They are life-saving in status asthmaticus.

The definition of status asthmaticus for the purposes of the Commonwealth Pharmaceutical Benefit Regulations is as follows: "A severe paroxysm of bronchial asthma, lasting more than 24 hours, which has proved resistant to recognized therapy and where life is endangered."

The safer, conventional drugs need not be discontinued with the initiation of steroid therapy.

Prednisone and prednisolone are the corticosteroids of choice in status asthmaticus because of their lessened mineralocorticoid action.

Maintenance corticosteroid therapy in the chronic asthmatic is contraindicated, and there is still some controversy regarding the relative importance of the potential harmful effects and the anticipated benefits. The effects of the preparation often diminish after a few months.

Intermittent inhalations of fine-particle hydrocortisone acetate powder are contraindicated if the patient is dangerously ill but have given prolonged benefit in some cases of recurrent asthmatic attacks. The proportion absorbed is probably considerable but much less than with oral or intravenous therapy, and therefore toxic effects are less. Optimum dosage for the inhalations is obviously difficult to determine.

Long-term therapy leads to complete suppression of supra-renal activity, and recovery of function is slow and unpredictable. Periodic stimulation of the adrenal cortex with exogenous ACTH is necessary if long-term corticosteroid therapy is undertaken.

When steroids are discontinued, the dose is gradually tapered off in decreasing amounts to allow the gradual recovery of the pituitary-adrenal mechanism.

General Principles of Steroid Therapy.—Steroid therapy is not a substitute for: (i) conventional management or (ii) safer drug therapy. Supervision and cooperation are essential. Parents should be aware of the dangers. The lowest possible dose should be used. Gradual tapering of dose is required. The dose is increased with stress. The large dose is given in the morning. Periodic adrenal stimulation is necessary.

Cortisone: Equivalent Dosages.—25 mg. of cortisone acetate is equivalent to each of the following: 20 mg. of hydrocortisone, 5 mg. prednisolone, 5 mg. prednisone, 4 mg. methylprednisolone, 4 mg. triamcinolone, 0.75 mg. dexamethasone.

PROPHYLAXIS.

Offending allergens should be removed.

Reassurance and rest should be provided if necessary.

Emotional exhaustion should be treated and the child's morale built up.

¹No. 3 of a series of synopses prepared by Dr. Alex Johnson in collaboration with the Australian College of General Practitioners. Each synopsis has been submitted for approval to a leading member of the College, to a professor of pharmacology and to a specialist in the field concerned.

Psychological, allergic and infective factors may all be interacting.

Sulphonamides may be given during the winter months to assist in prevention of respiratory tract infections, which are a cause of "intrinsic" asthma.

Mixed coryza vaccine is useful in some cases.

Personal hygiene may require attention, and over-protection may have to be corrected, but "toughening-up" must be undertaken sensibly and with care.

Desensitization may be indicated.

Rhino-pharyngeal surgery is of benefit on occasions, but tonsillectomy and adenoidectomy have a history of more failures than cures in asthma.

Concurrent disease should be treated.

Atopic dermatitis, commoner in bottle-fed babies, is a frequent forerunner of asthma.

Routine Immunization.—Routine immunization procedures (diphtheria, pertussis and tetanus) are not contraindicated in the asthmatic child, although, if atopic dermatitis is present, vaccination against smallpox should not be carried out.

ALEX JOHNSON.

British Medical Association.

ANNUAL MEETING, AUCKLAND, NEW ZEALAND, FEBRUARY, 1961.

THE one-hundred-and-twenty-ninth Annual Meeting of the British Medical Association will be held in conjunction with the Biennial Conference of the New Zealand Branch in Auckland, New Zealand, from February 6 to 10, 1961. This will be the first time the Annual Meeting has been held in New Zealand. Previous Annual Meetings held overseas were those at: Montreal, 1897, Toronto, 1906, Winnipeg, 1930, (jointly with the Canadian Medical Association); Melbourne, 1935; Toronto, 1955 (jointly with the Canadian Medical Association).

The President-Elect of the Association is Sir Douglas Robb, C.M.G., M.D., Ch.M., F.R.C.S., F.R.A.C.S., F.A.C.S. (Hon.), of New Zealand.

The Local Honorary Secretaries of the Annual Meeting are Peter Bartley, M.B., M.R.C.P., M.R.C.P.E., M.R.A.C.P., and Anthony F. Hunter, M.B., F.R.C.S., F.R.A.C.S., P.O. Box 3532, Auckland, New Zealand.

The Executive Officer of the Annual Meeting is Miss B. E. Middlemiss, B.M.A. House, Tavistock Square, London, W.C.1.

The New Zealand Branch has arranged an informal social programme for the weekend February 4 and 5, 1961.

The Annual Meeting will be officially opened in the Town Hall on Monday morning, February 6, by the New Zealand Minister of Health and the inaugural address will follow.

The adjourned Annual General Meeting will be resumed, and the presidential address will be held on Monday evening, February 6. The annual dinner will be held on Tuesday, February 7.

On Wednesday, February 8, conference members and their wives have been invited to spend the afternoon launching on the Waitemata Harbour.

The social programme will also include a late afternoon reception by the President and members of the Auckland Division, and the conference ball on the final evening. A full programme of excursions and entertainments will be arranged, and visitors from overseas will be the responsibility of individual New Zealand hosts.

The Annual Scientific Meeting from February 6 to 10, 1961, will include five plenary sessions devoted to the following subjects: Maintaining the health of the middle-aged executive. General surgical and medical and psychological problems occurring in pregnancy. Chemotherapy in cancer. Iso-immunization: A new concept of disease. Mental health in the community.

Round table conferences will be held on the following subjects: Thyroid disease. The present position of steroid therapy. Ulcerative colitis.

Programmes for the following fifteen scientific sections will be announced later: Medicine, Surgery, Obstetrics and

Gynaecology, Anaesthesia, Dermatology, General Practice, Neurology and Neurosurgery, Ophthalmology, Orthopedics, Otorhinolaryngology, Pediatrics, Pathology, Physical Medicine, Psychiatry, Radiology.

Scientific and pharmaceutical exhibitions will be held during the meeting.

Hotel Accommodation and Private Hospitality.

The tariff in the leading hotels in Auckland ranges from about 45s. to 65s. per day. This is usually inclusive of meals. Block bookings have been made for the period of the meeting, but reservations required outside these dates should be made as early as possible, as the meeting coincides with the tourist season.

Wherever possible, accommodation will be arranged in private homes in Auckland for visiting members who prefer this.

Application Forms.

Application forms may be obtained from the Secretaries of Branches.

Provisional Time-Table.

The provisional time-table is as follows:

Friday, February 3: Registration.

Saturday, February 4: 9 a.m.: Registration. 2 p.m.: Sport and social arrangements. 7.30 p.m.: Private entertainment by New Zealand hosts.

Sunday, February 5: Morning: Church services. 2 p.m.: Informal entertainment—picnics, etc. 8 p.m.: Theatre.

Monday, February 6: 9 a.m.: Registration continues. 9 a.m.: B.M.A. (N.Z. Branch) Council meeting. 9 a.m.: Opening of scientific and pharmaceutical exhibition. 11 a.m.: Opening of meeting by Minister of Health. 11.30 a.m.: Inaugural address. 2.30 p.m.: Plenary session. 8 p.m.: Annual General Meeting of the B.M.A. and Presidential Address.

Tuesday, February 7: 9.30 a.m. to 10.30 a.m.: Round table conference and scientific sections. 11 a.m. to 12.30 p.m.: Plenary session. 2.15 p.m. to 4.30 p.m.: Scientific sections. 7.30 p.m.: Annual dinner.

Wednesday, February 8: 9.30 a.m. to 11 a.m.: Plenary session. 11.30 a.m.: Excursion by launch.

Thursday, February 9: 9.30 a.m. to 10.30 a.m.: Round table conference and scientific sections. 11 a.m. to 12.30 p.m.: Plenary session. 2.15 p.m. to 3.30 p.m.: Scientific sections. 4.30 p.m.: Reception by the Auckland Division of the B.M.A. in the gardens of the Ellerslie Racecourse.

Friday, February 10: 9.30 a.m. to 10.30 a.m.: Round table conference and scientific sections. 11 a.m. to 12.30 p.m.: Plenary session. 2.15 p.m. to 3.30 p.m.: Scientific sections. 3.45 p.m.: Annual Meeting, B.M.A. (N.Z. Branch). 4.45 p.m.: War Memorial Oration. 9 p.m.: Conference ball.

VICTORIAN BRANCH: SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on May 6, 1959, at St. Vincent's Hospital, Melbourne. The meeting took the form of a series of clinical demonstrations by members of the honorary staff of the hospital. The first part of this report appeared in the issue of February 27, 1960.

Poikilodermatomyositis.

PROFESSOR J. G. HAYDEN showed a male patient suffering from poikilodermatomyositis, whose main symptom four years previously had been severe breathlessness and vascular changes in the fingers of Raynaud's type. On examination, he showed the signs of scleroderma and diffuse pigmentation of the skin, chiefly on the lower part of the abdomen and on the backs of the thighs and legs. Tiny spots of atrophy were present among the pigmentation. Skin biopsy confirmed the diagnosis. He was treated with cortisone; his breathlessness disappeared, and the pigmentation largely disappeared. At no time was there radiological evidence of pulmonary disease. The interesting feature was that four years previously he had been practically bed-ridden because of dyspnoea, but after treatment had earned his living as a clerk for four years.

Tuberculosis and Malignant Disease.

Professor Hayden's second patient was a woman, aged 29 years, who had presented herself in January, 1957, with pleuritic chest pain, cough, night sweats and vomiting, with

anorexia and loss of weight. She had had a similar illness two years before in Italy. On examination, she was found to be pale, with a right pleural effusion, vague abdominal fullness and a soft, irregular mass in the pouch of Douglas and right fornix, felt per vaginam; the response to the Mantoux test was positive, and cells which were characteristic of tumour cells were found on two occasions in the pleural fluid. No bacilli were grown.

Laparotomy revealed carcinomatosis peritonei with moderate ascites and a large amount of tissue in the position of the right ovary. Histological investigation revealed tuberculous tissue infiltrated by adenocarcinoma, probably ovarian, and many acid-fast bacilli were identified. A good recovery was made with treatment by streptomycin and isoniazid and a course of deep X-ray therapy to the abdomen. The patient was readmitted to hospital in September, 1957, with recurrent ascites, and a further course of radiation therapy was administered. An X-ray film of the chest was clear at that time. The patient remained well and gained weight. At the time of the meeting, the patient was free of symptoms and had gained three stone in weight, and no abnormal physical signs were detected.

Professor Hayden discussed the once popular theory of antagonism between tuberculosis and malignant disease, and said that the patient was shown to demonstrate that prognosis was not an exact art, and that all older practitioners had in their lifetime seen improvement and even cures which were unexpected. He quoted a similar case—that of a young man who was suffering from diffuse abdominal carcinomatosis, and who underwent two explorations by two different experienced surgeons, who stated that he was suffering from diffuse malignant disease. The diagnosis was confirmed by examination of sections. The patient was about and apparently well five years after the second exploration.

Subacute Bacterial Endocarditis.

Professor Hayden's third patient was a law clerk, aged 36 years, who had had St. Vitus' dance at the age of 13 years, and otitis media with intermittent discharge for 15 years. He gave a history of headache of four-and-a-half years' duration. Two years before his admission to hospital he had had an episode of meningitis with sterile cerebro-spinal fluid, and for a year had noticed crops of petechiae on his legs. A further episode of meningitis, again with sterile cerebro-spinal fluid, precipitated his present admission. He was found to have clubbing of the fingers, an aortic diastolic murmur, splenomegaly and a petechial rash on his legs. Two weeks after the commencement of treatment, he developed a typical Osler node. Examination of ear-prick blood smears revealed large histiocytes containing polymorphonuclear inclusion bodies. Professor Hayden said that that phenomenon had previously been described in cases of bacterial endocarditis, and occasionally in other septicemic states. As the patient's blood was persistently sterile, that finding was regarded as valuable supportive evidence in the diagnosis of subacute bacterial endocarditis. Similar findings had been detected in another patient with fever, splenomegaly and a loud mitral murmur, who improved on penicillin therapy.

Professor Hayden said that the length of history did not invalidate the diagnosis of subacute bacterial endocarditis, and he recalled one case, confirmed *post mortem*, in which without treatment the patient had survived for eight years, and had two cerebral vascular lesions during that period.

Systemic Lupus Erythematosus.

DR. HENRY BURGER demonstrated features of systemic lupus erythematosus by one case, together with autopsy material from two others.

The patient was a young woman, who three years earlier had developed peripheral oedema, pleurisy with effusion and ascites while resident in Italy. That condition completely cleared, and she had been well until a few weeks before her admission to hospital in April, 1959. On that occasion she again presented with peripheral oedema, ascites and a pericardial friction rub. The diagnosis of systemic lupus erythematosus was made when a white crescent-shaped area was noticed in the right fundus. That was regarded as a cystoid body. Dr. Burger said that those bodies had been reported in 16% to 20% of cases of systemic lupus erythematosus. The patient's condition improved spontaneously, and she was discharged from hospital well. No L.E. cells were demonstrated.

Dr. Burger then showed autopsy material from a truck driver, aged 58 years, who presented with symptoms and signs of renal failure, and a past history of pericarditis.

Photographs of the kidneys were shown, which demonstrated petechial haemorrhages throughout. Photomicrographs of the kidney showed focal thickening of capillary walls, the "wire loop" lesion. Those of the spleen showed the "onion-skin" lesion of periarteriolar fibrosis.

Two other specimens were from a school girl, aged 15 years, with a history of malaise, fatigue, weight loss and pleuritic chest pain. While an out-patient she was found to have numerous lupus cells in the blood, and was subsequently admitted to hospital with fever, vomiting, a maculo-papular rash on the cheeks, a pulse rate of 160 per minute and a pericardial friction rub. Despite massive steroid therapy, the patient died. *Post mortem*, changes of acute diffuse myocarditis were found, with thrombosed vessels, degenerate muscle fibres and inflammatory cell infiltration evident microscopically. Examination of sections of the kidney showed possible early "wire looping" of the glomerular capillaries. The patient also developed terminal hemolytic anaemia. Her Wassermann reaction was negative.

Right-Sided Staphylococcal Endocarditis.

DR. W. C. BOAKE discussed endocarditis. He said that lesions confined to the right side of the heart occurred in about 5% of all cases of bacterial endocarditis, and were often caused by staphylococci. He presented a case in which occurred the sequence of events characteristic of that condition—namely, staphylococcal septicemia, followed by the appearance of cardiac murmurs, followed in turn by the appearance of thin-walled cavities in the lungs. *Post mortem*, ulcerative lesions of the pulmonary and tricuspid valves were found, with normal aortic and mitral valves. Staphylococci of the same phage type as those found in the blood and sputum were isolated from the valvular lesions. Dr. Boake said that there were no signs of systemic embolization in the condition under discussion.

Polymyositis.

DR. J. J. BILLINGS first showed a middle-aged female patient, who presented with weakness of all the limbs, gradually increasing over a period of three months. At the end of that time there was severe paralysis of all the limbs associated with muscular wasting, the disability being most marked in the proximal muscle groups and being almost perfectly symmetrical. Muscle biopsy confirmed the clinical diagnosis of polymyositis, and a gratifying degree of recovery had followed treatment with prednisone.

Dr. Billings' second patient was a man, aged 40 years, in whom the same condition of polymyositis had developed rather more rapidly, but again had produced almost total paralysis, most marked in the limb girdle musculature, and associated with a papular erythematous eruption and some joint swellings, together with some sensory loss in the left upper limb. He, too, had improved remarkably after treatment with prednisone, and had now returned to work.

Basilar Artery Insufficiency.

Dr. Billings' third patient was a middle-aged man with basilar artery insufficiency resulting from stenosis of one vertebral artery, confirmed by arteriography. His attacks had virtually ceased on anticoagulant treatment.

Other Conditions.

Other patients shown were a boy, aged 16 years, with spinal compression from lymphosarcoma, and a man, aged 50 years, with Jacksonian epilepsy due to a secondary bronchogenic carcinoma.

Tuberculosis of the Knee Joint.

MR. T. KING showed a female patient, aged 27 years, who had presented herself in the out-patient department first in January, 1958, complaining of aching and swelling of her right knee present for six to seven months. On examination of the patient, the knee was swollen uniformly and was held in flexion, there being limitation of extension (15°); an effusion was present. Tenderness was present on the inner side of the joint line (the "hot spot"), and it was thought that she might have had an internal derangement of the knee (medial cartilage), the arthritis and effusion being secondary to this. However, in view of the long history, arthrotomy was considered wise. The Mantoux test produced a strongly positive response, but X-ray examination of the chest revealed no abnormality. A radiological examination of the right knee revealed soft-tissue swelling in the suprapatellar pouch and an exostosis on the medial tibial condyle. At arthrotomy, on April 2, the synovial membrane was found to be grossly thickened. The pathologist reported:

Tuberculosis of the knee joint. The synovial membrane is thickened due to the presence of epithelioid cells, giant cells, lymphocytes and in some a little caseation. No tubercle bacilli were demonstrated.

The patient was discharged, to the Austin Hospital, where she remained for six months (on chemotherapy); she was symptomless until three weeks after her discharge in October, 1958, when she fell and injured the knee. An effusion was present and there was some limitation of movement. X-ray examination revealed no change since January. She was again given chemotherapy—streptomycin (1 gramme every second day) and INAH (100 mg. three times a day for one month), to be reviewed then for changing to PAS. However, she did not appear again until April 26, 1959 in the out-patient department. She was then given the usual doses of the three drugs: (i) streptomycin, 1 gramme three times a week; (ii) PAS, 10 to 20 grammes per day; (iii) INAH, 300 mg. per day (100 mg. three times a day). Two drugs were used at a time, rotating at intervals of one, two or three months. Mr. King said that the knee had been splinted for six months whilst the patient was in bed, but she refused to use the walking caliper later. However, at the time of the meeting she had made a complete recovery in a short time, compared with the periods of years in the past before antibiotic therapy.

Avulsion of the Left Arm and Scapula; Dislocation of the Knee.

Mr. King's second patient was a male, aged 44 years, who had sustained a complete avulsion of the left arm and scapula. On March 11, 1959, he was involved in an accident in which a bucket caught his left arm and completely avulsed it. His body was pulled down and caused a complete dislocation of the knee. He was rushed 13 miles to hospital, and on arrival in the casualty department his systolic blood pressure was 70 mm. of mercury. Haemorrhage was occurring, but heavy dressings were preventing spurting. Fortunately, the subclavian vessels had not retracted although they were in spasm, and they were clamped with heavy artery forceps immediately on his arrival. Transfusion with Group IV Rh-negative blood was commenced. When his state of shock was halted, the large vessels were ligated and the wound was cleansed. It was not possible to close the skin edges as there had been too much skin loss. However, they were approximated to within two inches. An attempt was made to reduce the dislocated knee, but was not successful, although some improvement occurred. The leg was then placed in skeletal traction with a Steinman pin through the lower end of the tibia, on a Braun frame with 10 lb. of traction. This was especially to prevent sloughing in the area of skin which was pressed upon and stretched by the medially displaced medial condyle of the femur. He was instructed to move his left knee as much as he could while in traction. On April 14, one month later, open reduction of the left knee was carried out; the joint capsule was found to be "sucked into" the joint, preventing reduction. The situation was a replica of the coloured illustration in Sir Reginald Watson-Jones' textbook. As the patient had been moving the knee, adhesions were not present, so that it was a simple matter to extract the capsule with a hook; reduction thereupon took place. The defect in the capsule and vastus intermedius muscle was then repaired, and the leg was replaced on a Braun frame with a sling just below the knee to prevent posterior subluxation. Mr. King said that the patient had recovered from both injuries.

The Present Management of Diabetes Mellitus.

Dr. HAMILTON SMITH discussed the present situation of the management of diabetes mellitus with the newer insulins and tolbutamide tablets. He said that in his experience there was usually little to choose between isophane insulin and insulin zinc suspension (lente insulin), although infrequently when one of those insulins failed the other was successful. Occasionally the rather longer duration of action of the insulin zinc suspension (lente insulin) was an advantage. In 52% of his cases, one daily injection of isophane insulin alone provided satisfactory control, added regular insulin being required in 35%, and twice-daily injections with or without regular insulin being required in 5%. In 8% a change was made to another insulin. In 66% one daily injection of insulin zinc suspension (lente insulin) provided satisfactory control; added amorphous (semi-lente) insulin zinc suspension or crystalline (ultra-lente) insulin was required in 24%; twice-daily injections with or without added amorphous (semi-lente) or crystalline (ultra-lente) insulin zinc suspension were required in 4%. A change was made to another insulin in 6%. It was noted that of the rather large percentages of patients controlled by one

injection of either isophane or insulin zinc suspension (lente insulin) alone, most required only a small dose, and when the dose requirement approached or exceeded 28 to 40 units daily, addition of another insulin was usually required.

Dr. Hamilton Smith then discussed the use of tolbutamide tablets. He said that satisfactory control was obtained in 44 of 50 cases, but was not obtained in six cases. It was noted that the mean age in the successful group was 64 years, and that this was very much a selected group. No significant side-reactions were observed in that small series, in which the maximum maintenance dose used was 1.5 grammes per day. Failure to maintain control had been reported by some 5% to 10% of patients apparently well controlled for three to nine months on tolbutamide; but patients in his small series had been followed only for from three to 12 months, and relapse had not yet been observed.

Dr. Hamilton Smith's conclusions were that weight reduction alone, without either insulin or tolbutamide tablets, was adequate treatment for the over-weight diabetic; that with smaller dose requirements most patients could be controlled by a single daily dose either of isophane insulin or of insulin zinc suspension (lente insulin); that with larger dose requirements, most patients needed added regular insulin or amorphous (semi-lente) insulin zinc suspension, or occasionally twice-daily injections; that adjustment of diet might make the difference between good or poor control with either of those insulins; finally, that tolbutamide tablets frequently achieved good control in older diabetics whose diabetes first became manifest in middle or late age.

Ophthalmic Conditions of Medical Interest.

Dr. KEVIN O'DAY showed 14 ophthalmic patients to illustrate conditions of general medical interest.

The first two patients shown were suffering from retinitis pigmentosa. In one the condition was well developed, with marked tubular fields, night blindness, cataracts and the typical fundus picture, while in the second the condition was less advanced, and the fundus picture was the main diagnostic feature. The third patient had an advanced lesion; after a cervical sympathectomy, performed some years previously in an attempt to alleviate the condition, the patient had developed Horner's syndrome. A central posterior capsular cataract had now developed which, combined with the miotic pupil, had caused great loss of vision.

Dr. O'Day's next cases illustrated macular lesions. The first patient was a woman, aged 80 years, who showed gross senile macular degeneration, which had almost destroyed her central vision so that she was unable to read. The next patient was an aged woman with senile Coats's disease, in whom the macula in one eye had been replaced by a large, raised white mass of exudate, over which some abnormal blood vessels coursed. Two patients suffering from macular hemorrhages were shown. In the first the hemorrhage had been caused by a blow in the eye, and in the second it was associated with vascular hypertension.

Dr. O'Day then showed patients with optic disk abnormalities. The first was a young man with a congenital coloboma of the optic disk. The second patient had congenital opaque nerve fibres. The third had new blood vessels on the optic disk which had followed a thrombosis of the central retinal vein. Dr. O'Day then presented a young man with Leber's optic atrophy.

Dr. O'Day's final two cases illustrated keratoconus and senile ectropion.

Dermatological Conditions.

Dr. BASIL COLAHAN showed "Kodachrome" slides of several dermatological conditions.

The first case was one of the asthma-eczema syndrome of Besnier with a history extending over very many years. Periodic exacerbations of the patient's diffuse pruritic atopic neurodermatitis with marked flexural lichenification were controlled by prednisolone and sedation.

Transparencies were shown of an elderly male patient with two raised umbilicated lesions of the face, one at the inner canthus of the left eye and the other on the right infraorbital area. The two lesions had developed simultaneously, and had reached a diameter of 1.5 cm. within three weeks. A diagnosis of keratoacanthoma was acceptable in preference to squamous epithelioma. Three doses of X-ray therapy were given at intervals of two days, each of 400r, at 100 kilovolts, half-value layer 1.3 mm. of aluminium. The lesions had completely cleared in four weeks.

Dr. Colahan then described the case of a middle-aged female patient, who had presented herself several weeks

previously with a severe and diffuse intensely pruritic bullous eruption of the trunk and limbs. A diagnosis of Duhring's disease, dermatitis herpetiformis, was made, to the exclusion of pemphigus vulgaris. She had progressed extremely well with prednisolone (5 mg. three times a day), "Lederkyn" (500 mg. per day) and sedation, and when last examined was almost free from the eruption.

Two cases of Hansen's disease were next demonstrated, one of nodular type and the other of maculo-anæsthetic leprosy. Dr. Colahan said that in both instances the disease was extremely advanced and had obviously been present over a period of years. Swabs from the naso-pharynx, smears from ulcerative nodules and tissue excised for biopsy contained Hansen's acid-fast rod-like bacillus in profusion. Both patients had shown excellent response to "Dapsone". Dr. Colahan stressed the urgency of clinicians' becoming better acquainted with the clinical features of leprosy, as it was probable that Hansen's disease and other exotic diseases would be more frequently encountered in the future than had been their experience in past years, on account of the influx of migrants from countries where such diseases were endemic. Dr. Colahan expressed his thanks to Dr. McLorinan for making available the "Kodachrome" slides taken on the patients' admission to Fairfield Hospital.

Two slides were then shown in conjunction, the clinical pictures being practically identical. One was that of a young woman with psoriasis gyrata. She had evidence elsewhere of psoriasis apart from the lesion demonstrated, and her response to the complement fixation test was negative. The other patient had tertiary serpinous syphilide, one fixed single lesion of long duration and not pruritic. Her Wassermann reaction was strongly positive. Dr. Colahan pointed out the advisability of giving that patient a short intramuscular course of bismuth prior to administration of penicillin, to lessen the risk of a Herxheimer reaction.

Dr. Colahan then described the case of a young woman who had lupus erythematosus of chronic discoid type involving the face and ears, and who had attended the clinic intermittently over a period of some years. During that time she had received gold intravenously, bismuth intramuscularly, "Mepacrine" hydrochloride and more recently "Chloroquin". Any possible avenues of focal infection had been investigated in addition. Although she had shown very satisfactory response to treatment on two or three occasions, her affection had relapsed, and again she presented two or three fixed lesions.

Dr. Colahan then demonstrated a somewhat unusual variant of pemphigus involving the lips and buccal mucosa. He expressed the opinion that the prognosis closely approximated that of pemphigus vulgaris in its more common clinical form and was not a happy one. In the differential diagnosis, aphthous ulceration, secondary syphilis, lichen planus and Stevens-Johnson syndrome were discussed.

Dr. Colahan then showed slides of a male patient in late middle age, who had been examined during the year; the slides had been taken at varying periods in the development and course of his dermatitis. The primary clinical manifestations were multiple pruritic discoid eczematous lesions of the trunk, the upper parts of the arms and later of the face. His general health was sound and unimpaired, and at that early stage a diagnosis of endogenous discoid eczema or possibly parapsoriasis appeared acceptable. However, there had occurred progressive development of indurated tumours, one on the left lower part of the face approximately the size of a golf ball, which quickly showed necrotic ulceration. Sections were taken for biopsy, and after due deliberation it was suggested that the findings could be those of a dermal reticulosis, which in fact it was—mycosis fungoides. The administration of prednisolone and antibiotics proved futile. Temporary regression of the multiple tomato-like tumours was attained through the medium of X rays; but the end, which could not be long averted, occurred through toxæmia.

The Management of Burns.

Mr. R. K. NEWING showed patients and "Kodachrome" slides to illustrate various special points in the management of burns.

The first patient was a young man, who had suffered extensive fire burns to both legs whilst in an alcoholic stupor. The burns were circumferential, and were treated initially to exposure. However, when the patient was examined, the burn eschar had a tourniquet effect, and despite decompressing incisions along the full length of the legs, the anterior tibial muscles sloughed and liquefied. Mr. Newing emphasized the importance of early decom-

pression incisions in deep circumferential burns of the limbs. Another point illustrated by that patient was that Thiersch grafts would grow on cancellous bone. The whole of the anterior and lateral surfaces of one tibia were burned and mummified, with a widely-open knee joint and exposed medial meniscus. With time, however, the bone separated as a large sequestrum, and the granulating area was grafted satisfactorily. The knee joint was immobilized by a compression device, and firm ankylosis occurred. However, thicker grafts were necessary over the tibia for final durable repair, and that was in progress by means of abdominal tube pedicles migrated via the wrist.

Other patients were shown to illustrate the extent of scar contracture in burns. A boy, aged nine years, had a contracted burn scar behind the knee measuring 2 in. by 1.5 in. The defect required a dermatome graft 8 in. by 4 in. in area after excision of that scar. A mongol girl had grasped an electric radiator. The resultant scarring of the front of all the fingers tethered the pulps only one-quarter of an inch from the palm. A girl, with tight scars of the chest, at puberty, required the addition of extensive skin grafts to permit breast development. A man, aged 40 years, had had tight burn scars of the trunk for 30 years. The scars had never stretched, and recently had broken down to form an epithelioma—a Marjolin's ulcer.

Pancreatitis and Pancreatic Cyst.

Mr. T. ANTONIE showed patients to illustrate inflammatory conditions of the pancreas with cyst formation. He discussed with illustrations the various surgical techniques that might be employed in dealing with that condition.

Ulcerative Colitis.

Mr. Antonie then showed three patients with ulcerative colitis, in whom the disease was confined to an isolated segment of the large intestine. In each instance conservative resection of the bowel had been undertaken. In two cases, enteroanastomosis was performed and the necessity of an artificial anus was thus avoided. In the third case the condition was confined to the left side of the colon, and left hemicolectomy and anal excision were carried out. The patient had remained well over five years with a transverse colostomy, with its several advantages over ileostomy. All three patients were being kept under review for any possible extension of the disease to the remaining colon, and to exclude malignant change.

Myoma of the Stomach.

Mr. Antonie's next patient was a woman, aged 85 years, who had presented herself with hematemesis from a large myoma of the stomach which initially simulated a spleen and led to the diagnosis of portal hypertension. She had recovered well since the local resection of the stomach and tumour eight months previously.

Other Surgical Conditions.

Mr. Antonie then showed slides of (i) a case of spontaneous gas gangrene of the abdominal wall developing in a long-standing umbilical hernia, and (ii) A case of gall-stones and hydatid disease of the right kidney.

Premalignant and Malignant Skin Conditions Suitable for Radiation Therapy.

Dr. DENIS CLARKE gave a dermatological demonstration, illustrating by the use of transparencies those premalignant and malignant conditions of the skin which were suitable for treatment by radiotherapy. The contraindications were also stated. He said that keratoses, basal-cell carcinoma and squamous-cell carcinoma were frequently best treated by that method, although in certain cases plastic surgery, cautery or diathermy was preferable. Dr. Clarke pointed out that radiation therapy had nothing to offer in malignant melanoma. In most cases of premalignant conditions of the skin, cautery, diathermy, excision and the use of carbon dioxide snow were preferred, because of a subsequent need of radiation therapy or plastic surgery in the area. The dangers of ionizing radiations as employed by dermatologists were negligible, as the area treated and the depth dose were so small.

Anæsthetic Demonstration.

A demonstration comprising the following was arranged by the Department of Anæsthesia: (i) Fluothane: some apparatus currently used for its administration. (ii) Artificial respiration: the Bennet's respirator; inflation of the lungs with oxygen; mouth-to-mouth inflation using a plastic "resuscitator". (iii) Diagnosis of cardiac arrest; various forms of pulse and heart-rate indicators.

Out of the Past.

PUBLIC HEALTH.¹

[From the *Australasian Medical Gazette*, April 20, 1900.]

THE Bubonic Plague is now epidemic in Sydney. About 120 cases with 44 deaths were reported up to the 20th inst. Most of the cases have come from a limited area in the city on the shores of Darling Harbour.

Typhoid fever is now prevalent in Sydney and suburbs. During January and February there were 16 and 17 deaths respectively. In Hobart the deaths during these two months were 1 and 2. In Launceston, 1 in January. In Melbourne, 1 in January, 5 in February. In Brisbane 13 and 10. In Ballarat 5 and 2. In Auckland, there were 2 deaths from typhoid in January.

An Act for the proper supervision of the slaughtering of animals and the sale of meat, known as the "Meat Supervision Act 1900", came into operation in Victoria on the first day of March last.

There were only 13 deaths from diphtheria in Sydney and suburbs during the year 1899. There were during the same period 132 deaths from whooping cough, 87 from typhoid fever, 34 from puerperal fever, 353 from cancer, 70 from tubercular meningitis, 481 from phthisis, 282 from pneumonia, 380 from enteritis. There were 82 suicides and 18 murders.

Correspondence.

MEDICAL RESEARCH IN AUSTRALIA.

SIR: Your leading article on "Medical Research in Australia" and the list of research projects being undertaken is stimulating. It will no doubt lead to many more isolated pieces of research being discovered. The Mental Health Research Institute of Victoria, under the direction of Dr. Alan Stoller, has for some years been conducting various research projects in the mental hospitals of this State, including one into the mental health of older women.

Much is being done in this field in the United States of America, and at the International Congress of Gerontology to be held in San Francisco in August reports from many countries will be received.

I have been asked to speak briefly on the trends of research in gerontology in Australia, and have so far little information to give. Is there any work being done on this subject which might be mentioned at the Congress?

Yours, etc.,

VERNON DAVIES.

Mental Hospital,
Mont Park,
Victoria.
June 28, 1960.

SIR: Your editorial of June 25 refers to the encouraging improvement of medical research in Australia. After suffering for years from lack of organization and financial starvation, during which time it was barely kept alive by private benefactions and the contributions of overseas foundations, notably the Rockefeller Foundation, it was not until the Federal Government began to supply funds for medical research, and established first the National Health and Medical Research Council and later the Australian National University, that any real progress was made in the development of medical research in this country. More recently the Australian Universities Commission has been established. This presages not only further financial assistance for research to the universities, but a closer, welcome and long-overdue association between medical research and medical education.

The cause of the most recent and spectacular upsurge, however, has undoubtedly been the greatly increased financial support medical research has received from the general public by the formation of foundations, funds and similar trusts. Such bodies include the Cancer Council in Victoria, the Life Insurance Medical Research Fund of Australia and New Zealand, the Children's Medical Research Founda-

tion of the Royal Alexandra Hospital for Children, Sydney, the Laennec Society, the Post-Graduate Medical Foundation in the University of Sydney, and various other funds and agencies, including a Heart Foundation, shortly to be established, towards whose initial expenses the Federal Government has contributed the sum of £10,000.

Similar funds in other parts of the world have made signal contributions to medicine and to the stimulation of medical research. Some of them devote their attention to particular aspects of medicine, such as cancer, heart disease, tuberculosis, poliomyelitis and other disease and disabilities. Others, such as the Rockefeller and Nuffield Foundations, embrace all aspects of medical research.

Opposition to the special purpose foundations has at times been expressed by scientists and research workers abroad. Their objections have been that the channelling of funds into special objectives leads to an unequal distribution of research funds, and that oversubscription leads to the lowering of standards and duplication. Objection to the establishment of similar funds and their research activities in Australia is implied in the letter to you from Sir Macfarlane Burnet on January 6, 1960. In this letter he expressed concern at the multiplication of independent bodies making grants for research. He further suggested that before the appeal for the Heart Foundation be launched an immediate investigation be instituted. Sir Macfarlane also advocates that, apart from research directly associated with university teaching, the control of medical research in Australia should be centralized, that the allocation of research funds, whether governmental, public or private, should be placed in the hands of a central committee, something like the Medical Research Council, led by an executive head of high status, and that clinical research should be controlled by another committee working in close association with it.

Not everyone would agree with these proposals, particularly as there is every reason to believe that the present awakening of medical research in this country appears in no small measure to spring from opposite causes—from increased freedom, from decentralization and an escape from the very bonds with which Sir Macfarlane would again shackle it. The claims that only centralization will give the highest possible standards, and talk of "wasteful expansion" and "encouragement of the mediocre" need more than vague generalizations to sustain them. Central organizations are not invariably correct in their judgements. They cannot pick winners all the time, and decentralized committees may often be composed of men of no less ability. Examples of successful projects refused by central organizations are numerous. For instance, work on the Melrose Pump, which proved one of the outstanding successes in heart surgery, was first rejected by the Medical Research Council of Great Britain before it was supported by the Nuffield Foundation.

The suggestion in Sir Macfarlane's letter that committees that control foundations and trusts guide the lines of investigation which develop is true of very few, if any, of them, the usual practice being that lay members of these organizations concentrate exclusively on raising funds, whilst expert medical committees determine the grants.

The most serious effects of Sir Macfarlane's proposals would be on clinical research. This is a type of activity governmental organizations are often reluctant to support. Sir Macfarlane proposes that clinical research should be under the control of a special committee appointed by the Royal Colleges. But this type of research is *par excellence* the function of universities, particularly their departments of medicine and surgery, rather than of the Colleges, who have neither the finance, facilities or the universities' experience in research. To have the resources of clinical research pooled, as he suggests, or to have them controlled by committees in Canberra, in other States, or scattered throughout Australia is as unreal as it is impracticable.

Whilst there is likely to be strong opposition to any form of control, centralized or otherwise, agreement on the need for coordination could well be expected. Some degree of coordination in fact already exists between granting bodies, at least in New South Wales, where applications to one fund are at times referred to another. It is unrealistic to expect grants to be completely divorced from the policy of the granting body, whether government, university or foundation, and the establishment of some body or method to permit trading of grants between one organization and another might well be considered. At present, in most cases, one granting body usually knows already what other granting bodies are supporting and where similar work is being done.

One of the most important initial steps in the coordination of research in this country was the publication by you of

¹ From the original in the Mitchell Library, Sydney.

the report of the medical research activities in Australia and its supporting bodies in your issue of June 25. Australia in this respect might well follow the example of Canada, which achieves coordination by the yearly publication of a Reference List of Medical Research Projects for use in the administration and review of grants by the agencies supporting medical research in Canada. It is also important that all bodies making grants should regularly publish a detailed report of their grants and other activities.

The Post-Graduate Committee in Medicine in the University of Sydney is deeply interested in these subjects. It has associated with it a Post-Graduate Medical Foundation, whose lay members are concerned only with the raising of funds. Its research grants, travel grants and fellowships are made solely on the recommendation of expert committees derived from members of the Faculty of Medicine, the Post-Graduate Committee and leading research workers from research institutes and teaching hospitals. Distribution of funds is not confined to the University of Sydney or to New South Wales. Both the Committee and the Foundation are closely associated with other bodies with similar aims, some of whom it advises and assists.

Neither the Foundation nor the Post-Graduate Committee would at any time be prepared to pool its funds, submit to centralized control or hand over to others the direction of its policy or the allocation of its grants. In our opinion the new and exciting advances in medical research in this country have in no small measure been due to the generosity, interest and support of an increasing number of citizens, and that restrictions of the type proposed would seriously weaken local effort and prejudice this encouraging trend.

Unquestionably, there is a case for a strong central Medical Research Council. It would seem that this is the next step the Federal Government should logically take to advance medical research in this country by divorcing medical research from national health in the present National Health and Medical Research Council. But this body should be built on lines similar to those of the Medical Research Council of Great Britain, which lives happily with—without controlling—numerous foundations and similar bodies. The function of such a council should be to control Government grants for medical research, develop institutes and projects of its own, subsidise university departments, institutes and persons, but not to interfere with the work of universities or take control of the funds and activities of other bodies. Rather than centralized control, what is needed from such a council is the encouragement of independent thinking and of independent action.

No doubt some examination of our progress and adjustment to new ideas may be necessary; but let us not exaggerate our difficulties or allow doubts and unsupported generalizations check the welcome and valuable support that is now being given by the general public to the advance of medical research in Australia.

Yours, etc.,

131 Macquarie Street, V. M. COPPLESON,
Sydney. Chairman, Post-Graduate Committee in
July 6, 1960. Medicine in the University of Sydney.

THE ROYAL FLYING DOCTOR SERVICE AT "BROKEN HILL."

SIR: In an article on the work of the Flying Doctor Service at Broken Hill, published in the *Sydney Morning Herald* of Thursday, May 19, it is stated: "Sometimes he (the Doctor) has to detour to urgent calls, and the Section also has a second Drover Aircraft and a second pilot available for relief and emergencies."

I am going to contest this statement, because the Royal Flying Doctor Service is a service which I have thought about and worked for over a number of years. I resent anything in the nature of glamour or exaggeration that may be attached to that service. By the words quoted above, a wrong impression may be created in the mind of the public through the misunderstanding of a newspaper reporter who, in the short course of a visit to Broken Hill and a flight with the doctor, would not learn very much.

In what follows I am speaking only of the New South Wales Branch of the Royal Flying Doctor Service, which is centred at Broken Hill, and which is administered by a council in Sydney. There are eleven other bases scattered throughout Australia, and each base is autonomous. When I speak of the "network", I refer to the scattered inhabitants of the vast area around Broken Hill who call up the base at Broken Hill by radio. Most of them pay an annual fee to

belong to the service. (At the same time it is to be understood that nobody is neglected if in trouble, whether member or non-member and whether black or white.)

It is quite true that the Service pays two pilots and keeps a second "Drover" aircraft; but it is only partly true to say that a second pilot and a second "Drover" aeroplane are "available for emergencies". "Available" means always available (barring accident). This was not the case during my five years, and I doubt whether it is the case now. When I raised this subject back in 1956 to the member of the executive who seems to have always been their sole adviser in aviation, he insisted "This is a one-aeroplane, one-pilot service"—i.e., when one pilot is on duty the other is off. I continued to press the matter throughout my service, partly in order to get some relief from emergency calls for myself on those occasions when I had to go far afield to hold clinics on fixed dates. An "iron curtain" descended. The senior pilot remained completely free to fix days off duty as a private arrangement between pilots. They were free to leave Broken Hill by air or otherwise, and sometimes they did so. The executive in Sydney were ultimately responsible for this.

In early 1958 the chief pilot took one of our aircraft and five members of a British television team and absented himself from Broken Hill for over five weeks. The episodes enacted were primarily for display in Britain. The initiative of the chief pilot in this long usage of Service time and equipment in film work was endorsed by the executive in Sydney.

Each pilot is on a full award salary plus bonus for length of service. In the case of the senior pilot, there is also a free house and motor-car. Their position in fact is a good one and has been much sought after.

My present point is that employees of this service should always be available when wanted. If a pilot is away from Broken Hill flying a non-service aircraft, then he is not available. If he is in Broken Hill but cannot be located, then he is not available.

We did not often get caught out, because emergencies are not frequent, and double emergencies very infrequent. But it did happen. During a recent visit to Broken Hill I found a copy of a report of mine to the President in Sydney dated February 12, 1959, over one such case, and I quote from that report:

Owing to our slipshod arrangements here and owing to the lack of attention to requests made by me over the years [i.e., requests I had made to the Sydney Executive to have the pilots' duties properly rostered] I am of the opinion that we are not a first-class service, except as far as our radio work goes; and furthermore that we do not give the emergency cover to which people of this network are entitled, in return for the large amount of money invested in this Base and the large amount of money paid out in Salaries etc.

This happened six weeks before I flew to England on long-service leave. I had no reply to my report. It concerned a man with an acute abdominal condition. He was brought in by car 100 miles and operated on that night at Broken Hill Hospital. I was away on the Queensland border and had left a Broken Hill doctor in charge. He dealt with the case by radio and wanted to bring the patient in by air, as should have been done. But the "available" pilot was off duty, away in Adelaide, unknown to me. There had been earlier occasions, too. If my report was strongly worded, it should be remembered that it came after four years of frustration over this kind of thing.

In the financial year 1958-1959 flying salaries and flying costs amounted to £40 a day, as against £8 10s. a day to cover medical salary and expenses. The £40 represents running costs only. It does not take into account the huge sums invested in a hangar and in two three-engined "Drover" aircraft. The average flying time is light. That year it averaged only eleven hours a week, divided between two pilots.

The doctor, on the other hand, is on call seven days a week. The Service has become top-heavy at Broken Hill and over-centralized at Sydney. Too much emphasis is placed on flying and aeroplanes and too little on doctoring. It has become an ambulance service with a doctor attached.

In the 12 months since I left Broken Hill there have been no less than five changes of doctor. Unless the status of the Flying Doctor is raised, and unless more interest in and knowledge of his work is shown by an executive committee, and unless his reasonable requests are granted, there will continue to be a change of doctors every six to twelve months as there has been ever since Dr. Woods completed his great record of ten years, about 1946.

Finally, the Service at Broken Hill has been allowed to become associated with a commercial enterprise in the form of an air-taxi company, which has built its hangar alongside ours at Broken Hill airport. The position has become involved and has given rise to considerable criticism amongst local contributors and members of the network.

I believe that the only manner in which the above difficulties can now be solved is that a local executive committee should be appointed in Broken Hill. Men of the highest qualities are just as readily available in Broken Hill as they are in Sydney, and just as ready to give their services free, as the Sydney councillors do, to this important branch of social service in the far west of New South Wales.

Yours, etc.,

C. R. R. HUXTABLE.

Killara,

New South Wales.
June 28, 1960.

AUSTRALIAN MULTIPLE SCLEROSIS SOCIETY PHYSIOTHERAPY CLINIC.

SIR: I am writing at the request of the Committee of the Australian Multiple Sclerosis Society to make known to practitioners in this city, and indeed of this State, the facilities available at the physiotherapy clinic of this Society in Lytton Street, North Sydney, for the treatment not only of multiple sclerosis, but of all forms of spastic paraplegia. You were kind enough, Sir, to make known the excellence of this clinic some time ago; but I wish to reemphasize what can be done for patients suffering from multiple sclerosis, and paraplegics generally, by the trained and devoted physiotherapists attached to the staff. There is a hostel beside the clinic which can accommodate six patients, provided they are sufficiently mobile.

Brochures are obtainable from the Australian Multiple Sclerosis Society—7, Lytton Street, North Sydney, or 9, Clarendon Street, Vaucluse—which give all the details of the activities of the clinic and the methods of treatment available there. Some time ago the Society sent out a circular letter to some 1500 members of the profession in the metropolitan area informing them of the facilities available at the clinic and the types of patient who could be treated there.

Having witnessed what can be done for these disabled people, the Medical Panel of the Multiple Sclerosis Society wishes the benefits to be obtained from treatment at the clinic to be as widely known as possible.

I am, Sir, on behalf of the Medical Panel,

Yours, etc.,

K. B. NOAD.

135 Macquarie Street,
Sydney.
June 29, 1960.

GENERAL PHARMACEUTICAL BENEFITS.

SIR: At a recent British Medical Association (Victorian Subdivisional) meeting a number of motions were passed, condemning the present National Health Service and condemning all the people connected with this odious scheme. Many doctors would have nothing to do with the scheme. A challenge was issued for constructive criticism of how the scheme could be altered. One senior executive wisely pointed out that the public would object to the removal of the five shillings or similar low payment scheme. It is to be presumed that the five shilling payment is the Government's attempt to obviate the need for additional taxation.

Therefore may I suggest the following points, which could be implemented immediately.

For the medical profession: (i) That the doctor should (or will) prescribe freely (within reason) e.g., 20 instead of 12 x 250 mg. penicillin tablets, 4 or 6 injectable penicillin syringes and issue repeats of a similar quantity or less as thought fit. Suggest maximum three repeats. (ii) That all such incredible omissions as reserpine, "Largactil", etc., be instated. (iii) That the category "Specified Diseases" be retained mainly for guidance, and that the guidance should come only from the independent and excellent up-to-date antibiotic panels. (iv) That all or certain cortisone products, in particular topical ointments and sprays, be available as a special item at a cost to the patient of, say, one-third of the total, and the remainder be borne by the Government. (v) That all other sub-categories—e.g., additives, infants, pensioners—be omitted.

For the patient: (i) That the first and each fresh prescription should require a payment of five shillings. Repeats should require two shillings only. (ii) Maximum initial payment for two or more drugs for an individual should not exceed 10s. The same should apply to any family with, say, three children, who may each require one lot of the same drug. A charge of 2s. should be made for each repeat as above.

Yours, etc.,

R. WYATT.

Bulleen,
Victoria.

June 28, 1960.

The Royal Australasian College of Physicians.

VICTORIAN STATE COMMITTEE: LECTURE BY
DR. BRYAN HUDSON.

THE Victorian State Committee of The Royal Australasian College of Physicians has arranged for Dr. Bryan Hudson, of the Diabetic and Metabolic Unit, Alfred Hospital, Melbourne, to deliver a lecture on "Normal and Abnormal Patterns of Steroid Hormone Biosynthesis". The meeting will be held in the lecture theatre of the Royal Australasian College of Surgeons, Spring Street, Melbourne, on Thursday, August 11, 1960, at 8.15 p.m. All members of the medical profession are invited to attend.

Royal Australasian College of Surgeons.

ADMISSION OF NEW FELLOWS.

THE undermentioned, having satisfied the Court of Examiners, were admitted to Fellowship of the Royal Australasian College of Surgeons by the Council on June 23, 1960: Brian Maxwell Andrea, William Louthier Hunter Armstrong, Robert Britten-Jones, Donald Edmund Cam, Ross Campbell, John James Collins, Warwick John Cook, John Morton Copeland, Owen William Deacon, William Glasgow Ferguson, Martin Joseph Flood, William Douglas Friend, Jonathan Peter Halliday, Denis Graham Kermode, Stanley George Koorey, Harry Meldrum Leary, Hin Seng Leong, Selin Abraham Mellick, Archie Wilmot Middleton, John Patrick Richardson, Leo Rozner, Carille Herbert Schneider, Harry Danvers David Tyer, Marx Wald.

FACULTY OF ANÆSTHETISTS.

Admission of New Fellows.

THE undermentioned, having satisfied the Court of Examiners, were admitted to Fellowship of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons by the Council on June 23, 1960: James Loughman, Donald Charles Maxwell.

Notes and News.

Use of Live Poliomyelitis Vaccines.

THE Commonwealth Minister for Health, Dr. D. A. Cameron, has announced that it is not at present proposed to substitute oral live poliomyelitis vaccines for Salk vaccine in Australia. Dr. Cameron said that Salk vaccine had been proved both safe and remarkably successful. There was no reason, as yet, to believe that the oral live vaccines were as effective in all circumstances as Salk vaccine, nor was world opinion entirely satisfied that they were as safe, although experiments were highly encouraging in both respects. Dr. Cameron explained that the live vaccines taken orally subsequently multiplied in the bowel, from which they were likely to be excreted for a period of some six weeks. That multiplication in the bowel was held to confer two advantages lacking in Salk vaccine. Firstly, it was claimed that during that time, in addition to conferring a general immunity in the same way as Salk vaccine, the

virus created a local immunity in the bowel, which subsequently prevented the patient from becoming a symptomless carrier of poliomyelitis infection. Salk vaccine, being prepared from killed virus and given by injection, could not do that. Secondly, it was held that the escape of the attenuated virus from the bowel of the immunized subject was likely to lead to its spread to other persons to whom the vaccine had not been purposely administered. In that way large numbers of people who neglected to have themselves immunized would become immunized without their knowledge. However, Dr. Cameron said that there were two aspects of that multiplication of the virus in the bowel which occasioned disquiet. It had been shown that other viruses commonly circulating in the community, including virulent poliomyelitis virus, could outgrow the viruses of the vaccine and prevent them from immunizing effectively. Secondly, research to date had not eliminated the possibility that the virus of attenuated oral vaccines would not, after passage through the community, at some time revert to a type of virus which damaged the nervous system and caused poliomyelitis. Since live vaccine had now been given to millions of people without any recorded ill effects, that danger might be more theoretical than real; but until it had been conclusively disposed of, there was no point in accepting the risk in a community such as Australia, where the safe alternative of vaccination with killed virus was both convenient and practicable. Salk vaccine had produced remarkable results in Australia. Notifications had reached 4736 at the peak period in 1951. From 1952 to 1956 they had ranged between 1000 and 2000 a year. After the introduction of the Salk vaccination campaign in June, 1956, notifications had fallen to 125 in 1957. One hundred cases were notified in 1958 and 53 in 1959. To date in 1960 the number was 47. There was little doubt that there would have been even fewer cases had greater advantage been taken by adults of the mass immunization campaigns. Dr. Cameron said in conclusion that the Government was closely watching overseas research on live vaccines, and experiments were being conducted at the Commonwealth Serum Laboratories. Australia was in the happy position of possessing a vaccine which was known to be safe and effective. It would be most unwise to make any change while world opinion remained divided concerning both the safety and the comparative value of making general use of the live vaccines.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Examination Results.

The Post-Graduate Committee in Medicine in the University of Sydney announces that the undermentioned candidates satisfied the examiners at the recent examinations for Part II of the various medical diplomas of the University of Sydney as follows:

Anæsthesia: B. P. F. Mooney.
Dermatological Medicine: A. E. Cronin, W. J. Flood, B. Florance, J. H. Steele-Smith, R. M. Tipping.
Gynaecology and Obstetrics: F. C. Hinde.
Laryngology and Oto-Rhinology: B. B. Sheaves.
Ophthalmology: C. C. Burnside, L. F. Hann.
Psychological Medicine: J. S. Blow, J. A. Dobbie, N. Radziewsky.
Diagnostic Radiology: F. G. Harrison.

Course in Industrial Health.

The Post-Graduate Committee in Medicine in the University of Sydney announces that, in conjunction with the School of Public Health and Tropical Medicine, it will hold a full-time course in industrial health at the School from August 29 to September 16, 1960. The main subjects included in the course will be as follows: definition and scope of industrial health; historical aspects; activities in other countries and of international organizations; developments in Australia; organization, functions and responsibilities of Government departments and of private industry in relation to industrial health services; university teaching and research activities; duties and responsibilities of industrial medical officers; the working environment; recognition of occupational factors in disease and disability; psycho-

logical problems in industry; harmful substances: the effect of dusts, fumes, gases, mists and vapours; diseases caused by dust, metals, solvents, pesticides and other chemicals; dermatoses in industry; the prevention of occupational diseases; noise and occupational hearing loss; industrial ophthalmology; ionizing radiations: occupational and public health aspects; accident causation and prevention; rehabilitation and employment of disabled persons; industrial health legislation; introduction to laboratory equipment and procedures. In addition, visits will be made to factories and representative industries in order to study working conditions and processes related to these subjects.

The course is open to all interested medical practitioners, no fees being charged for attendance. However, written application is necessary, and should be made not later than August 15, to the Director, School of Public Health and Tropical Medicine, University Grounds, Sydney. Further particulars may be obtained from the supervisor of the course, Dr. Gordon C. Smith, at the School.

Annual Subscription Course.

The Post-Graduate Committee in Medicine in the University of Sydney announces that the following alterations have been made to the subjects of lectures to be given by Professor Bryan MacFarland, M.Ch.Orth., F.R.C.S., Professor of Orthopaedic Surgery in the University of Liverpool and official overseas lecturer for 1960 of the Australian Post-Graduate Federation in Medicine: Monday, July 18, 2 p.m., Students' Lecture Theatre, Royal North Shore Hospital—"The Causes of Limp in Childhood"; Wednesday, July 27, 8.15 p.m., Stawell Hall, 145 Macquarie Street, Sydney—"Common Fractures of Bone". In addition, Professor MacFarland will give the following lecture on the evening of Monday, July 25, at The Royal Newcastle Hospital—"The Causes of Limp in Childhood". The lecture at Sydney Hospital at 2 p.m. on Wednesday, July 20, entitled "Cervical Rib Syndrome", remains unaltered.

Week-End Course in Psychological Medicine.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course in psychological medicine will be held in the Scot Skirving Lecture Theatre of the Royal Prince Alfred Hospital on Saturday and Sunday, August 6 and 7, 1960, under the supervision of Professor W. H. Trethowan. The programme will be as follows:

Saturday, August 6: 2.30 p.m., welcome by Professor W. H. Trethowan, followed by "Methods of Mental Examination", Dr. John Shand; 3.15 p.m., "Common Diagnostic Problems in Psychological Medicine", Dr. John Ellard; 4.15 p.m., "Uses and Limitations of Medical Hypnosis", Dr. Martin Orne.

Sunday, August 7: 10.30 a.m., "Referral for Admission of Psychiatric Patients", Dr. J. G. Durham; 11.30 a.m., "Patterns of Illness in the Family", Dr. D. C. Maddison; 12.15 p.m., "The Management of the Elderly Psychiatric Patient", Dr. Ian Simpson; 2 p.m., "The Disturbed Adolescent", Dr. W. Wyatt; 2.45 p.m., "Attempted Suicide", Professor W. H. Trethowan; 3.15 p.m., panel discussion, "Any Questions?"

The fee for attendance is £3 3s., and those wishing to attend are requested to make early written application to the Course Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephone: BU 4497-8.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR AUGUST, 1960.

The Melbourne Medical Post-Graduate Committee announces the following programme for August, 1960.

Overseas Visitors.

The following are lectures which visitors from overseas will give for the Committee while they are in Melbourne:

Professor J. C. Goligher, F.R.C.S., of the Department of Surgery, University of Leeds, will lecture on "Early Diagnosis and Treatment of Cancer of the Rectum and Colon" on Monday, August 1, at 8.15 p.m., at the Royal Australasian College of Surgeons, Spring Street, Melbourne. Attendance is by a fee of 15s.; or annual subscription to the Committee.

Professor William Dameshek, M.D., haematologist, of Boston, will lecture on "Recent Advances in Clinical Haematology", on Thursday, August 4, at 8.15 p.m. at St. Vincent's Hospital new lecture theatre. Entrance is from Victoria Parade, through the Nurses' Home. There is no fee for this lecture, and all members of the medical profession are invited.

Mr. Norman Tanner, Consultant Surgeon and Surgical Tutor, of Charing Cross Hospital, London, will give the following lectures: Tuesday, August 9, "Surgery of Peptic Ulcer"; Thursday, August 11, "Hiatus Hernia"; at 8.15 p.m. in the Medical Society Hall. Attendance is by a fee of 15s. or annual subscription to the Committee.

Professor James Dauphinee, Professor of Pathological Chemistry, Toronto, will give two lectures, at 8.15 p.m. in the Medical Society Hall, as follows: Monday, August 15, "Plasma Proteins in Health and Disease"; Thursday, August 18, "Clinical and Laboratory Investigations of the Jaundiced Patient". Attendance is by a fee of 15s. per lecture or annual subscription to the Committee.

Country Courses.

Bendigo.—On August 5, at Bendigo Base Hospital, at 8 p.m., Dr. K. McCaul will speak on "Anaesthesia and Analgesia in Childbirth". The local secretary is Dr. M. Clark, 98 Mitchell Street, Bendigo.

Yallourn.—On August 13, at the Yallourn Hospital, the following course will be given: 2 p.m., "Hand Injuries", Mr. R. K. Newing; 5.15 p.m., "Low Backache", Mr. Bryan Keon-Cohen; 4.30 p.m., "Recent Advances in Genito-Urinary Surgery", Mr. J. B. Somerset; 8 p.m., "Common Eye Conditions: Diagnosis and Management in General Practice", Dr. Kelvin Lidgett. The local secretary for this course is Dr. J. E. Joseph, 237 Princes Highway, Morwell.

Ballarat.—On August 25, at Craig's Hotel, Ballarat, at 8 p.m., Dr. Glyn White will discuss "Causes of Stillbirth and Neonatal Deaths". The local secretary is Dr. I. C. Goy, 626 Sturt Street, Ballarat.

Warrnambool.—On August 27, at the Base Hospital, Warrnambool, the following course will be given: 3.45 p.m., "Methods of Promoting the Early Diagnosis of Cancer", Professor Maurice Ewing; 5.15 p.m., "Management of Jaundice", Dr. R. R. Andrew. The local secretary is Dr. R. Sobey, 6 Spence Street, Warrnambool.

Fees.—Fees for the above lectures are at the rate of 15s., but those who have paid an annual subscription to the Committee are invited without further charge.

Flinders Naval Depot.

On August 17, at Flinders Naval Depot, at 2.30 p.m., Dr. Peter Freeman will discuss "The Management of Deafness Resulting from Exposure to Loud Noise". This lecture is to be given by arrangement with the Royal Australian Navy.

Refresher Courses.

A paediatric refresher course will be held at the Royal Children's Hospital on August 29 to September 2 inclusive. The time table is now available from the Committee, and applications for enrolments, accompanied by the fee of £2 2s., should be sent to them by August 15. Details of the programme were given in this Journal last month. There is a special enrolment form.

A general practitioners' refresher course in medicine and surgery will be held at St. Vincent's Hospital on September 5 to 10. Details, now available from the Committee, will be published shortly. The fee is £9 9s.

A general practitioners' gynaecology and obstetrics refresher course will be held at the Royal Women's Hospital on September 12 to 23. Details of this course are also available and the Committee will publish them shortly. The fee is £14 14s., payable to the Committee, Board and residence at £7 10s. per week are payable to the Hospital.

COMING EVENTS.

The Committee draws attention to the following conferences, etc.

The Victorian Cancer Congress, from August 22 to 25, is to be conducted by the Anti-Cancer Council of Victoria.

The Conference on Post-Graduate Education, on August 10, 11 and 12, will be conducted by the Australian Post-Graduate Federation in Medicine, in Sydney.

Tutorials in Medicine are being conducted by the Faculty of Anaesthetists of the Royal Australasian College of Surgeons at the Alfred Hospital, Royal Melbourne Hospital and St. Vincent's Hospital, on Saturday mornings during July, August and September, one month at each hospital.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 11, 1960.¹

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2(2)	1(1)	..	1(1)	4
Anaebiasis
Ancylostomiasis	3	11	..	14
Anthrax
Bilharziasis
Brucellosis
Cholera
Chorea (St. Vitus)
Dengue
Diarrhoea (Infantile)	6(4)	8(8)	2(2)	1	1	18
Diphtheria	1(1)	1
Dysentery (Bacillary)	1(1)	1
Encephalitis	1(1)	1
Flariasis
Homologous Serum Jaundice
Hydatid
Infective Hepatitis	64(20)	17(16)	7(2)	13(8)	1	..	102
Lead Poisoning	1(1)	..	2	3
Leprosy
Leptospirosis	4	4
Malaria	1(1)	1
Meningococcal Infection
Ophthalmia	2	2
Ornithosis
Paratyphoid
Plague
Poliomyelitis	2	2
Puerperal Fever
Rubella	8(7)	..	4	1(1)	13
Salmonella Infection
Scarlet Fever	8(4)	11(10)	5(1)	3(1)	..	1	..	1	29
Smallpox
Tetanus
Trachoma	2(2)	..	6	..	8
Trichinosis
Tuberculosis	37(26)	19(15)	41(21)	5(4)	2(1)	1(1)	..	1	106
Typhoid Fever
Typhus (Flea-, Mite- and Tick-borne)
Typhus (Louse-borne)
Yellow Fever

¹ Figures in parentheses are those for the metropolitan area.

The fee may be ascertained from Dr. R. Clark, Convenor of the Sub-Committee of the Faculty.

ADDRESS.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne, C.I. Telephone, FB 2547.

Medical Practice.

REPRIMAND FOR VICTORIAN DOCTOR.

THE Medical Board of Victoria recently heard a charge of infamous conduct in a professional respect against a Melbourne suburban doctor for having improperly signed a number of Hospital Benefits certificates. The doctor was found guilty of the charge and was reprimanded by the Board.

The certificates concerned were Forms H.B. 17 and H.B. 18, which must be submitted by private hospitals when claiming Hospital Benefits payments. The evidence disclosed that a supply of blank certificates had been signed by the doctor and left in the possession of the proprietor of a private hospital.

In determining that such action on the part of a doctor constitutes infamous conduct, the Board considers that correct use of the forms concerned is of the utmost importance in safeguarding the administration of the Hospital Benefits Scheme.

Medical Appointments.

Dr. D. A. Hicks has been appointed Honorary Assistant Physician in charge of the Diabetic Clinic at the Royal Adelaide Hospital, Adelaide.

Dr. S. C. Milazzo has been appointed Honorary Visiting Medical Officer, Infectious Disease Section, Northfield Wards, at the Royal Adelaide Hospital, Adelaide.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Protopopoff, Nicholas Paul, M.D., 1917 (Univ. Odessa), licensed under Section 17b of the *Medical Practitioners Act*, 1938-1958, 41 King Street, Crow's Nest.

Nathan, Henry, M.D., 1951 (Univ. Sofia), licensed under Section 21(3), *Medical Practitioners Act*, 1938-1958, Institute of Medical Research, Royal North Shore Hospital, St. Leonards.

Nagy, Laszlo, M.D., 1944 (Univ. Budapest), licensed under Section 21c (4), *Medical Practitioners Act*, 1938-1958, 525 Hume Highway, Yagoona.

Brieger, Hans Hillel, M.D., 1921 (Univ. Breslau), licensed under Section 17 (2a) of the *Medical Practitioners Act*, 1938-1958, 1 Hume Avenue, Ermington.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Fromer, John Eugene, M.D., 1934 (Univ. Pisa), licensed under the provisions of Section 21a (Cassilis Region) of the *Medical Practitioners Act*, 1938-1958; Gould, Graham Roger, M.B., B.S., 1957 (Univ. Sydney); Roche, James Barry, M.B., B.S., 1956 (Univ. Sydney); O'Malley, Terence, M.B., B.S., 1959 (Univ. Sydney); Macken, James Ernest, M.B., B.S., 1959 (Univ. Sydney).

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association:

Chan, Mary Mei Li, M.B., B.S., 1959 (Univ. Melbourne). Hoffman, Mervyn John, M.B., B.S., 1959 (Univ. Adelaide).

Deaths.

THE following deaths have been announced:

CORNFORD.—William Henry Hall Cornford, on June 24, 1960, in Queensland.

ALLEN.—Malcolm Norman Allen, on June 30, 1960, at Melbourne.

QUINLAN.—Daniel Alphonsus O'Connor Quinlan, on July 2, 1960, at Perth.

Diary for the Month.

JULY 18.—Victorian Branch, B.M.A.: Finance Sub-Committee.
JULY 19.—New South Wales Branch, B.M.A.: Medical Politics Committee.

JULY 20.—Victorian Branch, B.M.A.: Clinical Meeting (Alfred Hospital).

JULY 21.—New South Wales Branch, B.M.A.: Clinical Meeting.

JULY 21.—Victorian Branch, B.M.A.: Executive Meeting of Branch Council.

JULY 22.—Queensland Branch, B.M.A.: Council Meeting.

JULY 26.—Tasmanian Branch, B.M.A.: Southern Subdivision.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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